NORTH CAROLINA

Medical Journal

Vol. 18 No. 11
November, 1957

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THIRD PARTY ENCROACHMENT
PRESIDENT EDWARD W. SCHOENHEIT

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NORTH CAROLINA MEDICAL JOURNAL

Official Organ of

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NUMBER 11

NOVEMBER, 1957

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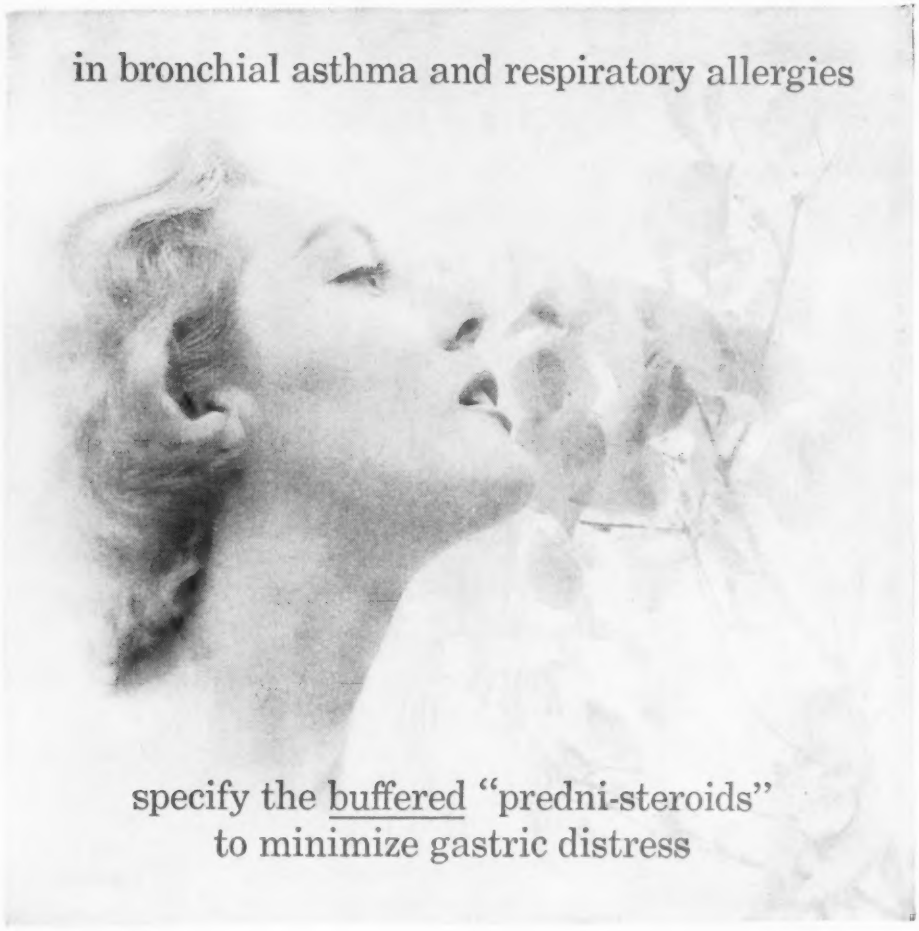
in bronchial asthma and respiratory allergies



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Flu Fight

Drug Firms Speed Up Vaccine Output, But Will the U.S. Need It

Asiatic Virus Raises Threa
Government Buys, Proc
nd Hens Have to Help

en Attack, Rapid Sprea

8 STUDENTS ON FLIGHTS TO U. S. HAVE ASIAN FLU

New York, Aug. 15 (
Laboratory tests on e
foreign exchange student
arrived Aug. 8 show they
victims of Asiatic flu, the
health department repo
today. The eight arrived
plane from Europe.

Twenty-nine other stud
suffering from influenza
rived Tuesday from Rot
dam on the ship Arosa Sky.
One, Nicholas Memmos,
Greek exchange student, dic
yesterday. Six of these stu-
dents were released today
the others are to be r
tomorrow. It has not
termined whether
died from Asiatic

THE INFLUEN

How Deadly Will it Be
What Can We Do abou

IF Y

Answe

A new
—is showi
around the
now have

The War on Mutant A

If Florence was in the grip of an epidemic of colds, coughs and fevers, astrologers . . . declared that it was caused by the influence of an unusual conjunction of planets. This sickness to be known as "infl
—Chronicles of
1200-1470.

To combat new
fluence," a worldwide
this week in respons
from the Far East. S
is the World Health
neva, which collects i
from around the globe
specimens of the ene
tions. In more than a
including those of th

Asian Flu: the Outlook

Asian influenza will hit the U.S. this fall before mass immunization can be effective, and the nation faces an epidemic which may strike 15 million to 30 million people. The disease is relatively mild (in no way comparable to the killing "Spanish flu" of 1918-19), and is likely to cause only a small number of deaths among the feeble young and enfeebled old. But it may compel 10% to 20% of the population in affected areas to tak
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U.S. Fighting As

The War On Asiatic Flu

There's cause for concern about Asiatic flu, but scientists and public health officials see no reason for anyone to panic.

First shipments of the vaccine against the new influenza strain have arrived in Chicago, setting off a flood of telephone calls from worried patients to doctors, and from doctors to drug suppliers. This is a norm
pattern of mass fear and is understan
The of the

Even though Salk vaccine priorities were necessary, the regulation produced administrative headaches, public complaints and probably a gray, if not a black market. When regulation
invoke it.
would

PUBLIC HEALTH

Influenza M

➤ INFLUENZA, one of the most unp
dictable of communicable diseases, is re
ing "on cat feet" across the nation rig
now. It has already struck once this ye
in mild epidemic form at an Air For
base in Colorado. When and how severe
it will strike again is a perennial riddle
public health authorities.

It will probably not lie dormant f
the rest of the winter months. At the lea
there will be sporadic outbr
throughout the country. If

to counteract
complications from

"ORIENTAL FLU"

IDEMIC
Is Causing It?

CATCH "ASIATIC" FLU—

ut the New Virus Threat From Orient

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filmtab®
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CASE SUMMARY[2]

Amenorrhea of 4 years' duration in a 24-year-old married woman. A course of 10 mg. NORLUTIN twice daily for 5 days was followed after 3 days by menses lasting about 5 days. Since no spontaneous menstruation occurred during the following 35 days, she was given another course of treatment with NORLUTIN, 10 mg. twice daily for 5 days. This was followed by menses.

When this patient was given ethisterone, 40 mg. twice daily for 5 days, no bleeding had ensued when she was seen 41 days later.

INDICATIONS FOR NORLUTIN: conditions involving deficiency of progestogen such as primary and secondary amenorrhea, menstrual irregularity, functional uterine bleeding, endocrine infertility, habitual abortion, threatened abortion, premenstrual tension, and dysmenorrhea.

PACKAGING: 5-mg. scored tablets (C. T. No. 882), bottles of 30.

REFERENCES: (1) Greenblatt, R. B.: *J. Clin. Endocrinol.* **16**:869, 1956. (2) Hertz, R.; Waite, J. H., & Thomas, L. B.: *Proc. Soc. Exper. Biol. & Med.* **91**:418, 1956.

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» unexcelled antihistaminic action

Diagnosis	No. of Patients	Response				Side Effects
		Excellent	Good	Fair	Negative	
Allergic rhinitis and vasomotor rhinitis	30	14	9	5	2	Slight Drowsiness (3)
Urticaria and angioneurotic edema	3	1	1	1		Dizzy (1)
Allergic dermatitis	2		1	1		Slight Drowsiness (2)
Bronchial asthma	1		1			
Pruritus	1		1			
Total	37	15	13	7	2	Drowsiness (5) Dizzy (1) 16.2%

From the preliminary **Dimetane Extentabs** studies of three investigators. Further clinical investigations will be reported as completed.

DIMETANE® EXTENTABS® TABLETS ELIXIR

DIMETANE IS PARABROMDYLAMINE MALEATE – EXTENTABS 12 MG., TABLETS 4 MG., ELIXIR 2 MG. PER 5 CC.

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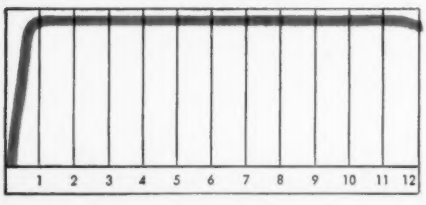

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Meat...

in the congestive phase of cardiac disease

Meat fits well into the moderate-protein, restricted-sodium, acid-ash diet currently recommended for many patients with congestive cardiac failure.[1]

The protein of meat—in the proportionate arrangement of its essential amino acids—closely approaches the quantitative proportions needed to promote human tissue synthesis and repair. For this reason lean meat proves important in maintaining positive nitrogen balance without excessive protein intake.

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The acid ash of meat aids in the promotion of diuresis.

The easy digestibility of meat is a prime requisite of foods specified for the patient with congestive cardiac disease.

In addition to these important features, meat contributes other nutritional factors essential in any convalescence —the B vitamins thiamine, riboflavin, niacin, pantothenic acid, B_6, and B_{12}, and the minerals iron, phosphorus, potassium, and magnesium.

1. Odell, W. M.: Nutrition in Cardiovascular Disease, in Wohl, M. C., and Goodhart, R. S.: Modern Nutrition in Health and Disease, Philadelphia, Lea & Febiger, 1955, p. 699.
2. Bills, C. E.; McDonald, F. G.; Niedermeier, W., and Schwartz, M. C.: Sodium and Potassium in Foods and Waters, J. Am. Dietet. A. *25*:304 (Apr.) 1949.

The nutritional statements made in this advertisement have been reviewed by the Council on Foods and Nutrition of the American Medical Association and found consistent with current authoritative medical opinion.

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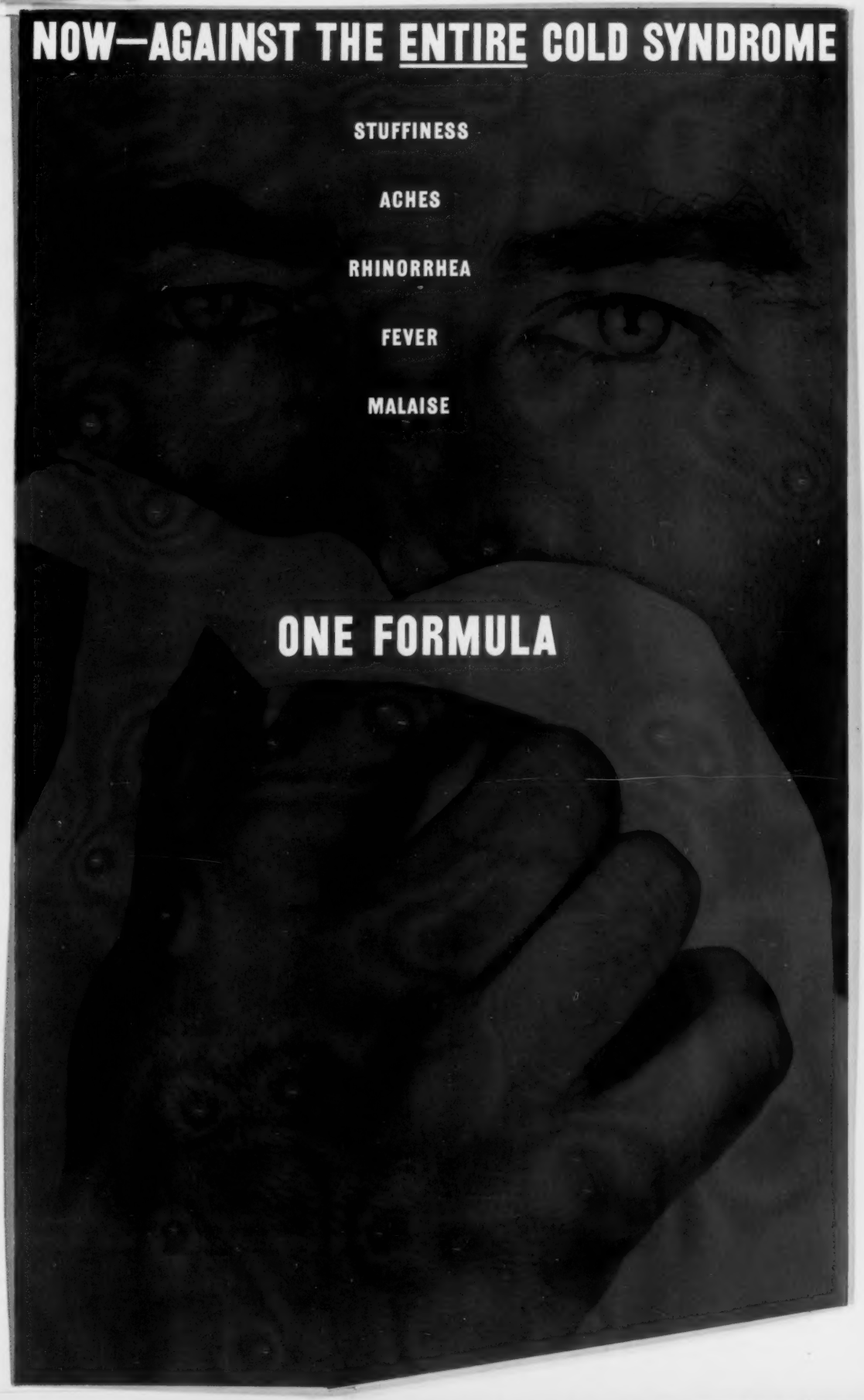

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CONTROL OF COMMON COLD SYMPTOMS with

Neo-Synephrine Compound Cold Tablets
is pharmacologically comprehensive
and clinically practical...

COMPREHENSIVE because this new
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Neo-Synephrine hydrochloride...5 mg.
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effective, well-tolerated antihistaminic

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Caffeine...15 mg.
dependable, mild, stimulating agent

DOSAGE:

Adults—2 tablets three times a day

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1 tablet three times a day

Bottles of 100 tablets

TO CLEAR THE AIRWAY

topically
in colds,
sinusitis
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NTZ®

Nasal Spray

quick
and
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Combining three effective intranasal medications, NTZ produces sustained decongestion ...aeration...sinus drainage. There are virtually no side effects; and NTZ maintains therapeutic action throughout repeated use. The NTZ squeeze bottle is convenient and simplifies adherence to prescribed procedure.

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when anxiety and tension "erupts" in the G. I. tract...

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Combines Meprobamate (*400 mg.*) the most widely prescribed tranquilizer . . . helps control the "emotional overlay" of gastric ulcer — without fear of barbiturate loginess, hangover or habituation . . . *with* PATHILON (*25 mg.*) the anticholinergic noted for its extremely low toxicity and high effectiveness in the treatment of many G.I. disorders.

Dosage: 1 tablet t.i.d. at mealtime. 2 tablets at bedtime. *Supplied:* Bottles of 100, 1,000.

*Trademark ®Registered Trademark for Tridihexethyl Iodide Lederle

Lederle

LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, NEW YORK

New Chemotherapy

ARALEN® *in* RHEUMATOID ARTHRITIS

Extensive studies of rheumatoid arthritis and related collagen diseases—in this country and abroad—have shown the antimalarial Aralen phosphate to be highly effective and well tolerated in a large percentage of patients.

Clinical Results with Aralen in Rheumatoid Arthritis

Author	No. of Cases	Major Improvement	Minor Improvement	No Effect
Haydu[1]	28	22	5	1
Rinehart[2]	25	12	4	9
Freedman[3]	50	43	3	4
Bagnall[4]	108	77	12	19
Bruckner[5]	36	22	0	4
Cohen and Calkins[6]	22	17	3	2
Scherbel et al.[7]	25	9	8	8
Total	294	212 (72%)	35 (12%)	47 (16%)

- Success dependent upon persistent treatment
- Often of benefit where other agents have failed
- Remissions on therapy well maintained
- Remission of 3 to 12 months possible even if treatment is interrupted
- Tachyphylaxis not evident

GENERAL EFFECTS:

- Patient feels better
- Patient looks better
- Exercise tolerance increases
- Walking speed and hand grip improves

LABORATORY EFFECTS:

- E. S. R. may fall slowly
- Hemoglobin level may gradually rise

ANALGESICS AND STEROIDS:

- Requirements usually reduced or eliminated

JOINT EFFECTS:

- Pain and tenderness relieved
- Mobility increases
- Swellings diminish or disappear
- Muscle strength improves
- Rheumatic nodules may disappear
- Even severe or advanced deformity may improve
- *Active* inflammatory process usually subsides
- Joint effusion may diminish

DOSAGE:

Aralen is cumulative in action and requires four to twelve weeks of administration before therapeutic effects become apparent.

Latest information indicates that an initial daily dose of 250 mg. of Aralen phosphate is preferable to the higher doses sometimes recommended. However, if side effects appear, withdraw Aralen for several days until they subside. Reinstate treatment with 125 mg. daily and, if well tolerated, increase to 250 mg. The usual maintenance dose is 250 mg. daily.

New Chemotherapy

INDICATIONS:

- Rheumatoid arthritis, acute or chronic —with or without adjunctive therapy.
- Spondylitis
- Arthritis associated with lupus erythematosus or psoriasis

THEORY OF ACTION:

Aralen appears to suppress or induce remission of rheumatoid inflammatory processes by inhibiting adenosinetriphosphatase.

HOW SUPPLIED:

Aralen phosphate: 250 mg. tablets in bottles of 100 and 1000.
125 mg. tablets in bottles of 100.

Tolerance:

Aralen is usually well tolerated. Toxic effects are usually mild and to date have been transitory in nature, disappearing completely either on continuance or cessation of therapy or on reduction in dosage.

Gastrointestinal disturbances (e.g. nausea, rarely vomiting, diarrhea, abdominal cramps, anorexia) are frequent manifestations of intolerance. Temporary blurring of vision (due to interference with accommodation) is also relatively frequent.

Pleomorphic skin eruptions (e.g. lichenoid, maculopapular, purpuric), although generally mild, may preclude the use of an optimum dosage schedule. If a skin reaction persists on a reduced dosage schedule, or recurs after reinstitution of treatment with gradually increasing doses, discontinue Aralen till the lesion again disappears and consider resuming treatment with Plaquenil® (brand of hydroxychloroquine).

Less frequently transitory vertigo, headache, lassitude, or neurological disturbances, such as nervousness, irritability, emotional change, and nightmares have been reported. Instances of unexplained slight gradual weight loss as the patient's general health and arthritic condition improved have been mentioned. Occasional instances of bleaching (depigmentation) of the hair have been described.

Although an occasional instance of leukopenia, with normal differential count, has been reported (WBC about 3000), it has not proved troublesome because it has always been reversible on discontinuance, or diminution of the dose. Even spontaneous reversal may occur while full dosage is maintained.

Caution:

Aralen is known to concentrate in the liver and, although hepatic damage has never been reported, the drug should be used with caution in the presence of liver disease. In the presence of severe gastrointestinal, neurological, or blood disorders, the drug should be used with caution or not at all. If such disorders occur during the course of therapy, the drug should be discontinued. Concomitant use of gold or phenylbutazone with Aralen should be avoided because of the tendency of these agents to produce drug dermatitis.

Clinical Comments:

Of fifty patients receiving Aralen therapy, "43 have become really well; that is, they have no stiffness, and any pain that occurs can reasonably be attributed to use of joints affected by secondary degenerative changes. They have no evidence of joint inflammation, but may have a raised erythrocyte sedimentation rate. They have little or no need for analgesics." *Freedman*[3]

"One hundred and twenty-five private patients have been carefully followed clinically and haematologically while receiving well over 200 patient-years of chloroquine [Aralen] therapy. The results are considered good in 70%, one-half of these cases being in remission. Improved work performance, sedimentation rate, and hemoglobin levels paralleled the major objective gain in this 70%. 90% of them remained on chloroquine [Aralen] therapy, half for more than two years. Classical peripheral rheumatoid arthritis, spondylitis, arthritis of juvenile onset, and rheumatoid disease with psoriasis, all appeared to respond about equally well.

"It is suggested that chloroquine comes closer to the ideal for long-term, safe, control of rheumatoid disease than any other agent now available." *Bagnall*[4]

"Out of the 36 rheumatoid arthritis cases we treated . . . favorable results were obtained in 32 cases. *Bruckner et al.*[5]

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7. Scherbel, A. L., Schuchter, S.L., and Harrison, J.W.: Comparison of effects of two antimalarial agents, hydroxychloroquine sulfate and chloroquine phosphate, in patients with rheumatoid arthritis, *Cleveland Clin. Quart.* 24:98, April, 1957.

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Each teaspoonful (5 cc.) contains:

ACHROMYCIN® Tetracycline equivalent to tetracycline HCl	125 mg.
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Ascorbic Acid (C)	25 mg.
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CARTRAX should be taken *before* meals, on a *continuous* dosage schedule. Use with caution in glaucoma.

1. Russek, H. I.: J. Am. Geriat. Soc. *4*:877 (Sept.) 1956.

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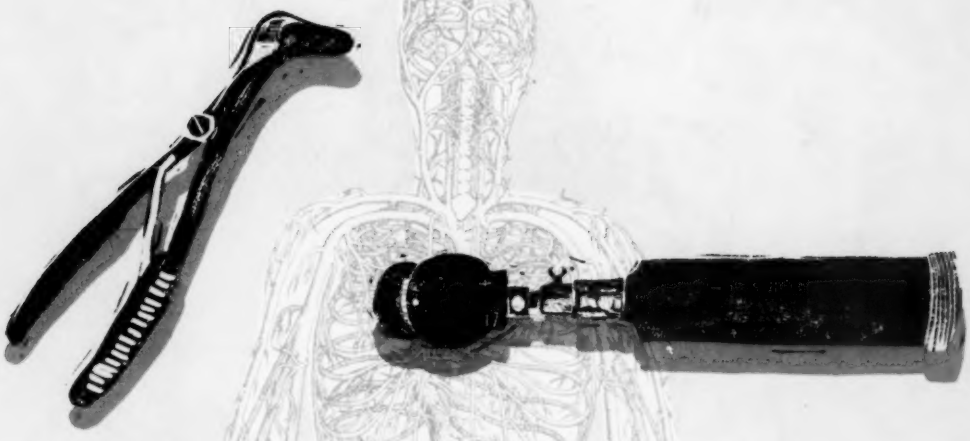

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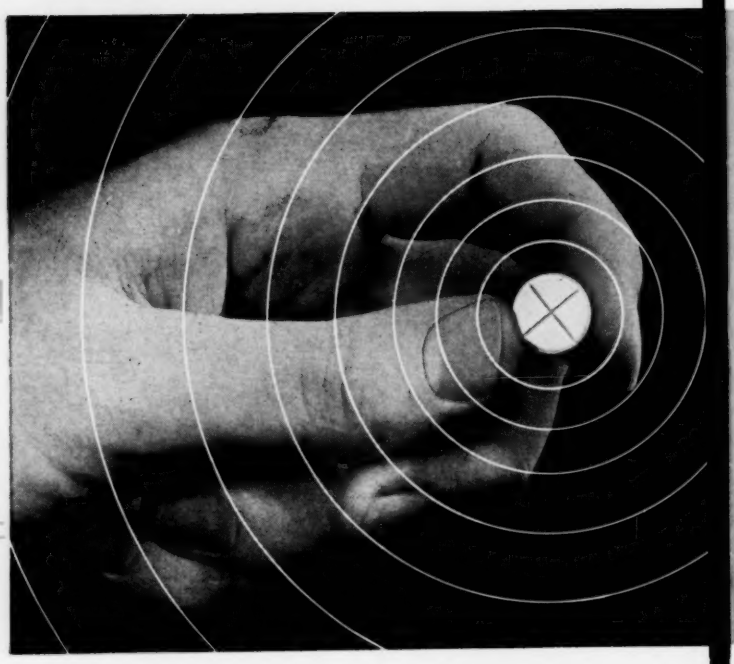

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The recommended adult dose is 1 Gm. (2 tablets or 4 teaspoonfuls of syrup) the first day, followed by 0.5 Gm. (1 tablet or 2 teaspoonfuls of syrup) every day thereafter, or 1 Gm. every other day for mild to moderate infections. In severe infections where prompt, high blood levels are indicated, the initial dose should be 2 Gm. followed by 0.5 Gm. every 24 hours. Dosage in children, according to weight; i.e., a 40 lb. child should receive ¼ of the adult dosage. It is recommended that these dosages not be exceeded.

Tablets:
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Syrup:
Each teaspoonful (5 cc.) of caramel-flavored syrup contains 250 mg. of sulfamethoxypyridazine. Bottle of 4 fl. oz.

[1] Nichols, R. L. and Finland, M.: J. Clin. Med. 49:410, 1957.

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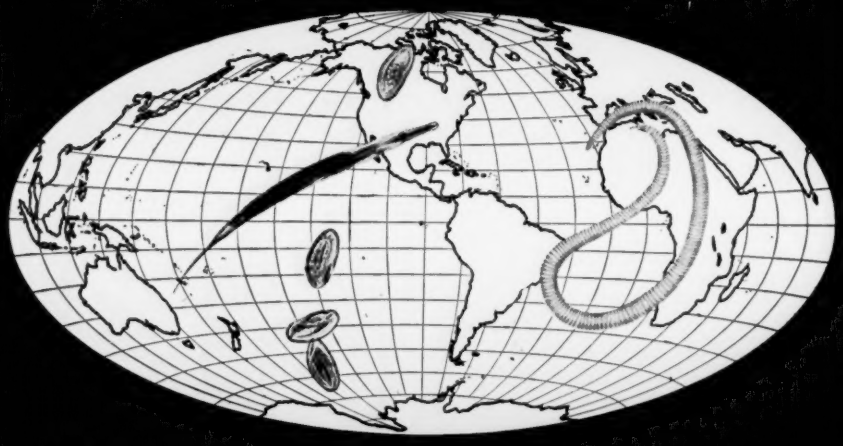

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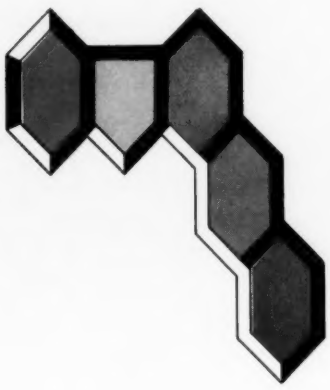
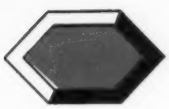
Harmonyl has also demonstrated its potency and relative freedom from side effects in hypertension. In a study comparing various forms of rauwolfia[2], the investigators reported deserpidine "an affective agent in reducing the blood pressure of the hypertensive patient both in the mild to moderate, as well as the severe form of hypertension." They also noted that side reactions were "less annoying and somewhat less frequent" with this new alkaloid. Other studies confirm that few cases of giddiness, vertigo or sense of detached existence or disturbed sleep are seen with Harmonyl.

Professional literature on this unique rauwolfia derivative is available upon request. Harmonyl is supplied in 0.1-mg., 0.25-mg. and 1-mg. tablets. Abbott





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Lewis, H. H.: Frumess, G. M., and Henschel, E. J.: Rocky Mountain M. J. 54:806 (Aug.) 1957.

"Results of treatment with oleandomycin-tetracycline of 50 infections [mostly respiratory] due to resistant organisms and 40 infections [respiratory, skin, urinary infections] due to sensitive organisms are very encouraging. In some of these patients, [Signemycin] was lifesaving, and in others surgery was made unnecessary. This confirms other reports."

Shubin, H.: Antibiotic Med. & Clin. Therapy 4:174 (March) 1957.

Based on case reports documented by independent investigators in 26 countries abroad, the clinical response obtained with Signemycin in 1404 patients with a wide variety of infections was successful in 1329 patients; in 13 cases only was it necessary to discontinue therapy because of side effects.

Report on 1404 Cases Treated with Signemycin: Medical Department, Pfizer International. Available on request.

In 50 nonselected patients, Signemycin "...appears to be effective in the treatment of most general surgical infections, including virulent staphylococcus aureus infections. In some cases these infections had been clinically resistant to other antibiotics. The drug is apparently well tolerated."

Levi, W. M., and Kredel, F. E.: J. South Carolina M. A. 53:178 (May) 1957.

Of 50 patients with various infectious processes, 26 had not responded to previous antibiotic therapy. With Signemycin "Ninety-six per cent of the mixed infections were clinically controlled. . . . and in none of the cases was there any reason to discontinue the drug."

Winton, S. S., and Chesrow, E.: Antibiotics Annual 1956-1957. New York, Medical Encyclopedia, Inc., 1957, p. 55.

Signemycin in 79 patients with severe soft tissue infections: "The average response of these cases was excellent and inflammatory symptoms subsided with almost uniform rapidity....The magnitude and incidence of surgical intervention was reduced....Side reactions were minimal. . . ."

LaCaille, R. A., and Prigot, A.: Antibiotics Annual 1956-1957. New York, Medical Encyclopedia, Inc., 1957, p. 67.

Five groups of patients (total 211) with acne were treated with one of five antibiotic agents, including Signemycin (55 cases). "The results were evaluated taking into consideration the usual response to such conservative conventional therapy and the rapidity of response." In 8 weeks, Signemycin rapidly attained and maintained the highest percentage of efficacy of antibiotic agents tried.

Frank, L., and Stritzler, C.: Antibiotic Med. & Clin. Therapy 4:419 (July) 1957.

In the treatment of 78 patients with tropical infections, some complicated by multiple bacterial contamination or present for years, Signemycin was found to be "...an exceptionally effective agent," requiring smaller doses and less extended periods of therapy than with the tetracyclines alone, and "caused no notable toxic reactions."

Loughlin, E. H., and Mullin, W. G.: Antibiotics Annual 1956-1957. New York, Medical Encyclopedia, Inc., 1957, p. 63.

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"Thiosulfil" is rapidly absorbed and excreted, achieving high antibacterial levels in the urine and throughout infected tissue, with negligible penetration into red blood cells.

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"Thiosulfil," in both the active and acetylated forms, is highly soluble in urine over a wide pH range, thus permitting effective action with minimal side effects. Alkalinization is not required; fluids may be restricted rather than forced.

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"Thiosulfil" is virtually unacetylated. As much as 90-95 per cent remains in the free therapeutically active form. Virtually all of a given dose is therefore available for antibacterial action.

In a long-term clinical study, patients with incurable chronic urinary infections were kept symptom free for as long as five or six years on a maintenance dose of one or two tablets of "Thiosulfil" daily.[4] In another evaluation, 20 patients were given 25-100 grams of "Thiosulfil" over a period of 20-90 days without incidence of side reactions.[5] Goodhope[6] reports that during 30 months of clinical use with "Thiosulfil," no evidence occurred of exanthemata, urticaria, emesis, fever, hematuria and crystalluria.

Recommended Dosages: 0.5 Gm. four times daily. The pediatric dosage is 30 to 45 mg. daily per pound of body weight. If voiding occurs during the night, an extra half-dose should be given. Fluids may be restricted rather than forced.

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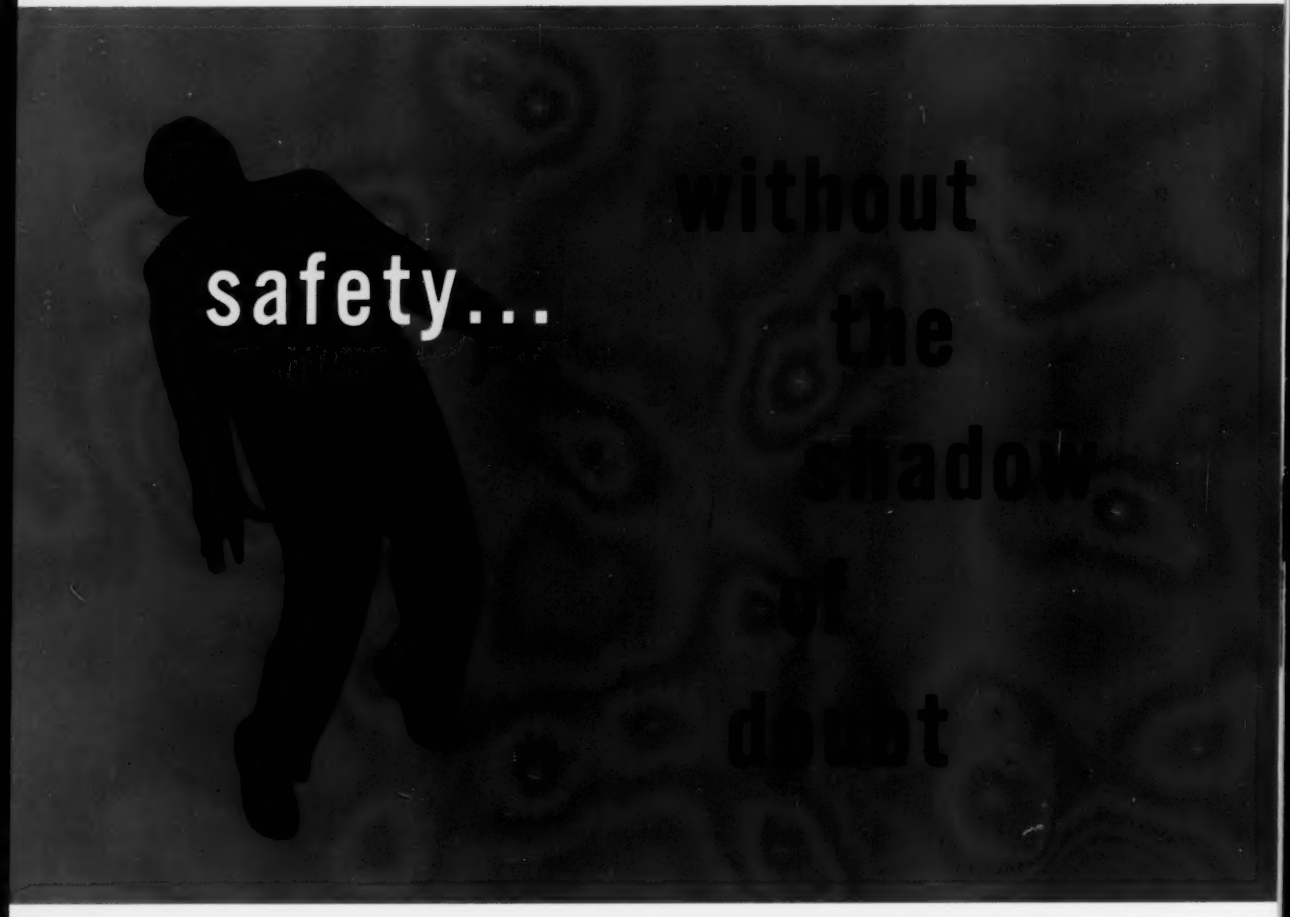

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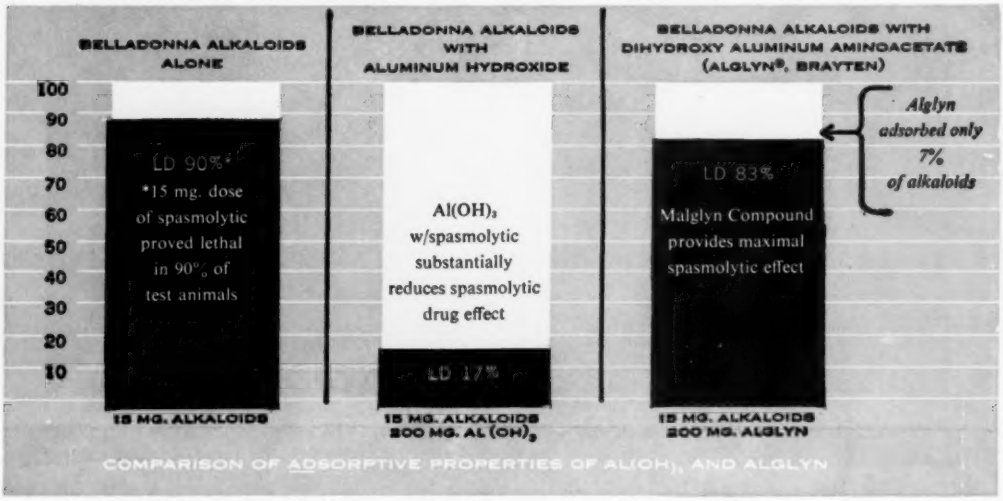

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belladonna alkaloids (as sulfates)	0.162 MG.
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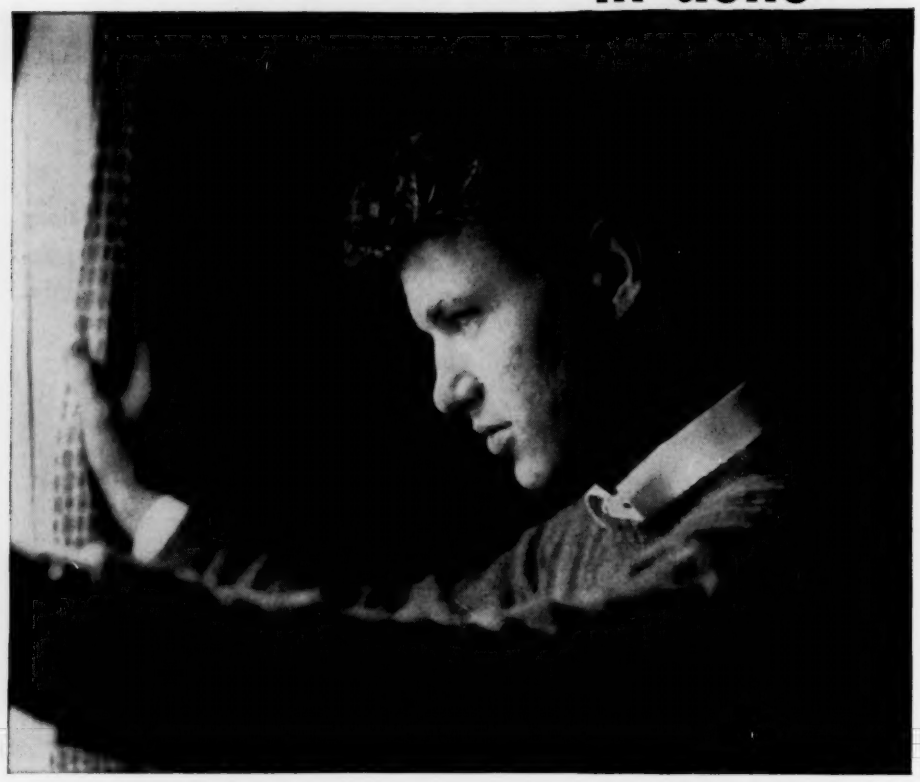

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1. Hodges, F. T.: GP, *14*:86, Nov., 1956.

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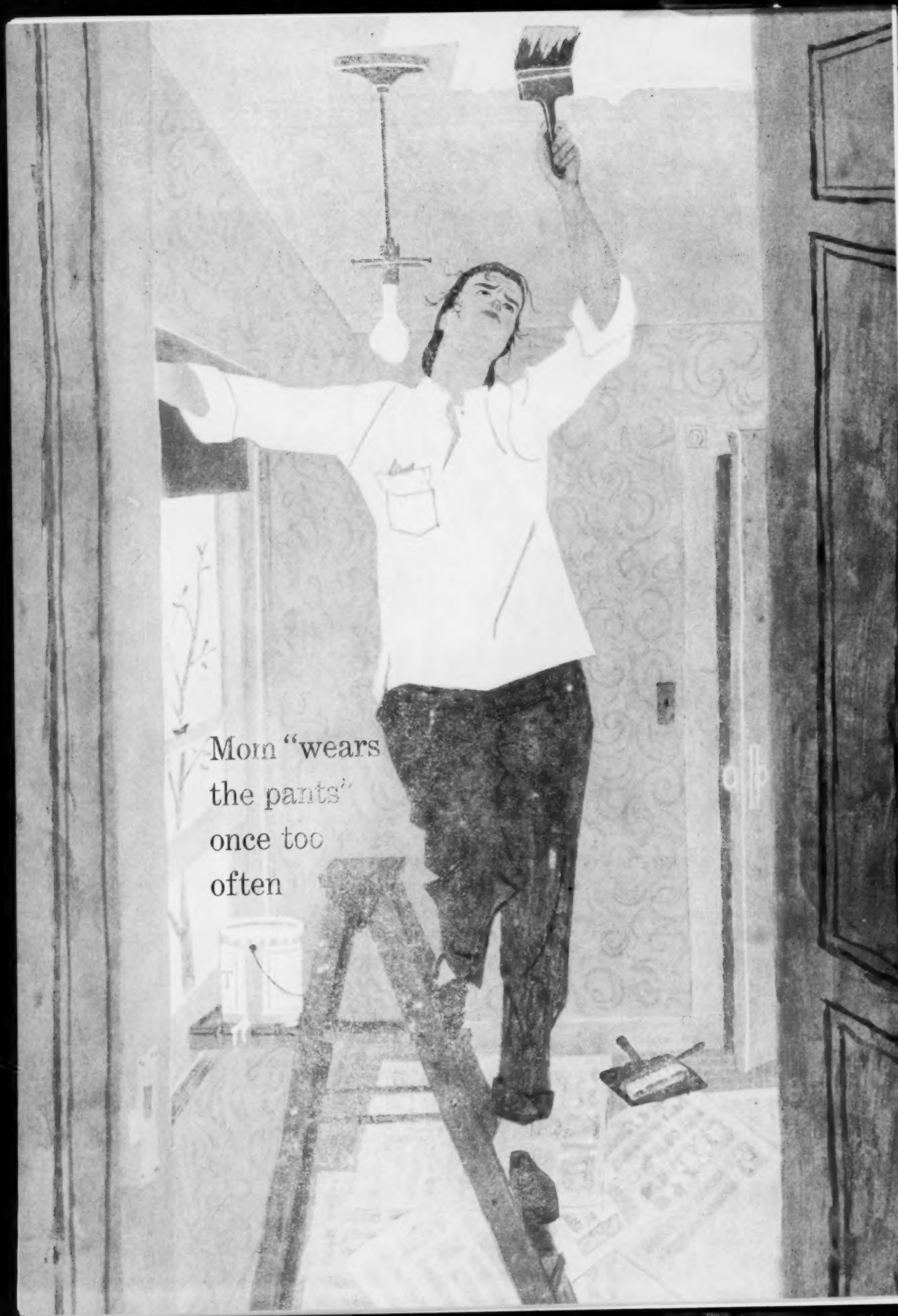
Mom "wears
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once too
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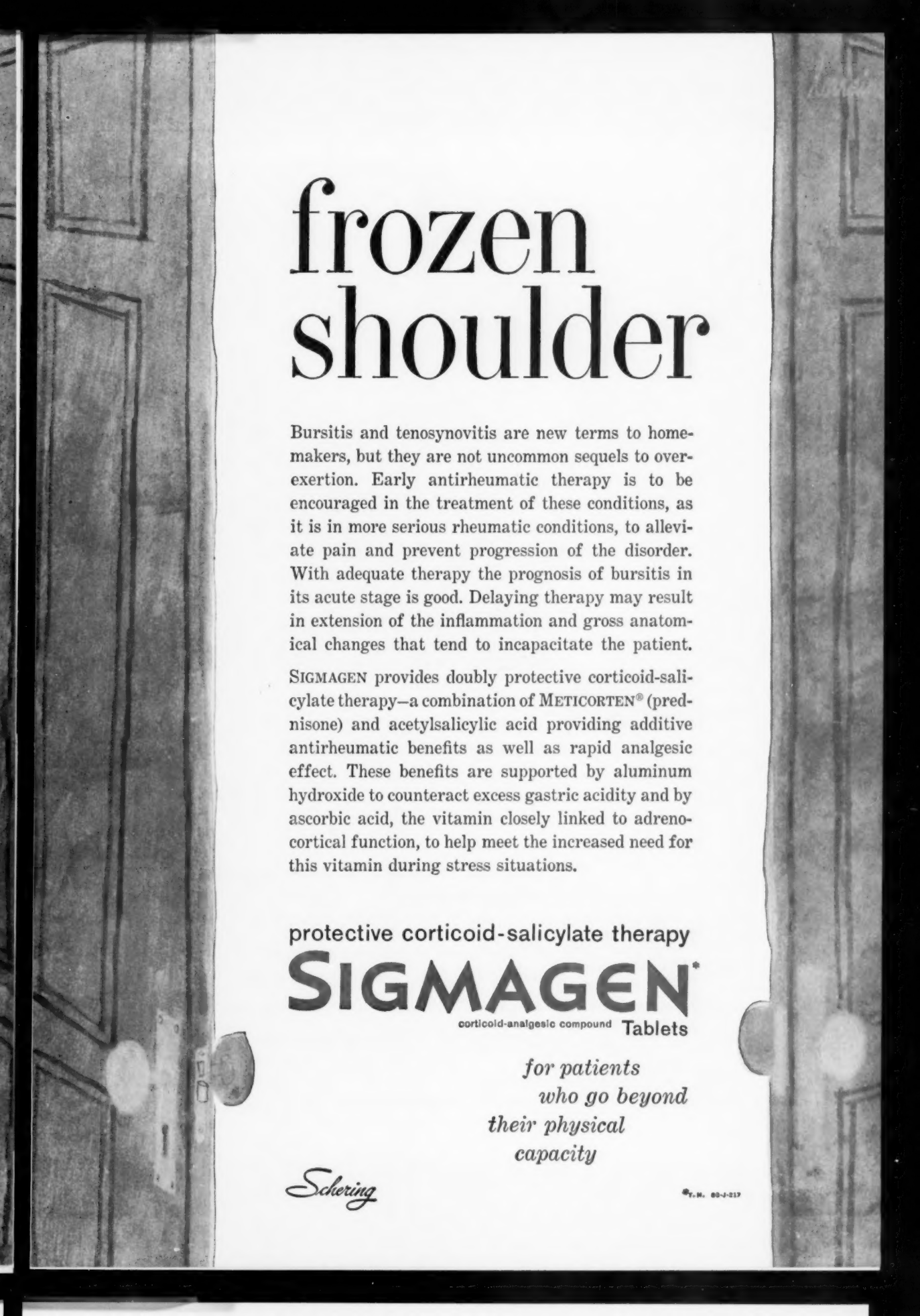

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Current Comments on Influenza

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Influenza, an illness of medical importance for several centuries, is again a significant topic among various medical specialties. We have been noting for some months a world-wide outbreak termed Asian influenza, the name having been derived from the area of origin.

General Outbreak

In order to put the present disease into its proper perspective it seems desirable to discuss briefly the background of epidemic influenza. For approximately 400 years epidemics and occasionally pandemics are now known to have occurred. Descriptions of influenza epidemics go back as far as 1500. In 1580 a pandemic was recorded. Hirsch reports that between 1800 and 1875 55 large outbreaks, of which 8 were pandemics, occurred. In our own United States the first large pandemic occurred in 1758. There were pandemics in 1782 and 1889-1890. Many individuals alive today were ill of that latter disease.

A special note relative to the 1918-1919 outbreak seems indicated, since so much of our present fear of influenza is derived from the experience obtained during the first World War and the year immediately following. At that time influenza was seen in three distinct waves, the second of which was an extremely severe one, characterized by a high mortality rate. The first cases were seen as early as 1915 or 1916, but certainly by 1918 much of the United States and the world as a whole, except for a few isolated areas, were involved. The estimated total number of cases in this country was 20 million, with approximately 850,000 deaths due to the disease. In our Armed Forces, which were particularly hard hit, about 50,000 members died. An estimated 20 million died throughout the world.

The particularly high mortality of the 1918-1919 outbreak was in striking contrast to previous epidemics and pandemics. In the earlier instances the disease primarily attacked children under 10 years of age. When deaths occurred they were largely in the very young and the relatively few elderly patients who became ill. In the 1918-1919 pandemic severe illness occurred during the "prime of life." Deaths, while not confined solely to the 20-40 year age group, occurred in greater numbers in that particular group. In this respect, then, the 1918-1919 pandemic was very different from outbreaks previously recorded.

Influenza Viruses

The influenza viruses have been placed into four distinct groups, A, B. C, and D. Viruses of the A and B types have been responsible for epidemics and pandemics. Subdivisions of the family of influenza viruses are based upon differences in antigenic structure. Study of antigenic structure has now revealed four strains of influenza A virus. The first of these, swine influenza virus, was isolated in 1931, and in 1933 the first of the influenza viruses found to be definitely pathogenic for humans was discovered by Smith, Andiewes and Laidlaw. This strain was labeled "Influenza Virus A." A variant of the swine infllluenza is believed by some to have been

Read before the Sixth District (North Carolina) Medical Society, Chapel Hill, October 9, 1957.

*State Health Officer and Assistant Director, Epidemiology Division, North Carolina State Board of Health.

the causative agent of the 1918-1919 pandemic. The A group appears to have been in circulation through 1943.

In 1947 a new strain of A influenza viruses made their appearance. These were labeled "A prime strains." A prime strains produced influenza outbreaks in a more or less regular two or three-year cycle from 1947 until last year. Indeed, some of our present outbreaks in the Western United States are being produced by the A prime influenza strains today. A fourth strain of A influenza viruses began to appear in 1956 and were most strikingly demonstrated early in 1957. Late in 1956 a new strain of A virus was isolated in Holland, and early in 1957, at Denver, Colorado, an influenza A strain was isolated which was quite different from any of the A prime strains previously identified. This brings us to the present situation, caused by the so-called "Asian influenza virus," which is a variant of the A family and very different in antigenic structure from any of its predecessors. It may not be the first time, however, that this virus (or one of similar make-up) has appeared on the scene, since certain elderly individuals residing in Europe have been demonstrated to have antibody to this agent. These data are interpreted to mean that a virus of like antigenic structure has caused infection before and may possibly have been the causative agent in the pandemic of 1889-1890.

Asian Influenza

Let us now review the present influenza picture, beginning with the outbreak in Hong Kong in April of this year. Information coming out of North China indicates that as early as January, 1957, large outbreaks were taking place in that region, with progressive spread to Peking and Canton in March of this year. Very rapidly the disease spread to Singapore, Formosa, Borneo, Japan, the Philippines, Malaya, and Hawaii. The virus was introduced into Holland by air travellers.

As had been predicted, the influenza virus was not long in arriving in the United States, though in certain outbreaks its actual mode of transmission remains unknown. In particular, the first outbreak documented in this country occurred among members of the fleet in Newport, Rhode Island. Illness was seen late in May and early in June. To date, however, no light has been shed as to the ultimate source of the Asian virus in the outbreak. Within a very few days the illness was also encountered in San Diego, California, having been introduced by service personnel from the Pacific area. From this point it spread rather rapidly through the state of California. Large outbreaks occurred in various military and civilian camps in that state.

A large encampment of young people at Grinnell, Iowa, however, served as the focus from which Asian influenza was first disseminated throughout most of our states. A girl who had attended a camp in California, where there was much influenza-like illness, attended the encampment at Grinnell, Iowa. Very shortly thereafter, of the 1,700 students attending, some 200 became ill of an influenza-like illness. The approximately 1,700 students were housed in dormitories intended for 900 students. Crowding, incident to such an arrangement, may have been a factor in rapid spread of the illness. Decision was made to care for the ill at Grinnell and to permit the well to go home. A large number of the young people returning to their homes became ill en route, and additional individuals became ill after arriving at their destinations. Thirty-nine young people from North Carolina attended the meeting. Shortly thereafter another gathering of 53,000 Boy Scouts took place at the Jamboree in Valley Forge, Pennsylvania. Two contingents from California showed appreciable illness on arrival. The Boy Scouts were bivouacked two per tent, an arrangement which is not ideal for the rapid spread of respiratory disease. The gatherings in commissaries and places of entertainment where the Boy Scouts were closely packed together, however, did permit rapid transmission of the influenza virus. About 600 Scouts became ill of what was later shown to be Asian influenza, then scattered to their home destinations, spreading the virus.

Ordinarily, influenza spreads rapidly only in winter months. In Australia, however, only limited spread has occurred in the cold months. In sharp contrast, Japan, located in a temperate zone, showed rapid spread of the disease in the summertime. Influenza

may spread rapidly in the tropics at any time.

Clinical Description

Despite the difference in agents, the disease itself differs in no way from the outbreaks of influenza previously seen — with the exception of the 1918-1919 outbreak, which, as you know, was of a much more severe nature than outbreaks occurring either before or since. The incubation period is from one to five days. Most cases will occur from one to three days after exposure. Onset is sudden, with severe headache, pain in the eyes, back and legs, and general malaise. Fever, while ordinarily ranging from 101-102 F., may rise to as high as 104 or 105 F. Cold-like symptoms are a constant feature. The fever lasts from two to five days; a feeling of general weakness persists for from 2 to 14 days or more. The laboratory findings are not striking. Leukopenia is the only rather constant feature. When complications occur, however, the white blood cell count may be expected to rise.

Treatment

Treatment is nonspecific and supportive. Patients should be advised to go to bed and to call the family physician. The use of antibiotics is contraindicated except in unusual or complicated situations which must be judged on their own merits. In some instances physicians will wish to give antibiotics as a protective measure to the very young, and possibly the very old, who are severely ill. Antibiotics may also be indicated in patients who are suffering from chronic or debilitating cardiac and pulmonary disease of non-allergic nature. Generally speaking, hospitalization is not indicated. Hospitals may show populations of antibiotic resistant *Staphyloccoci*, which pose special problems for influenza patients. The severely ill and those with complications will, of course, require hospitalization. At the present time it is impossible to give the rate that complications may be expected to occur.

Mortality

Less than 20 deaths associated with Asian influenza have been reported in this country at this writing. Each death appears to have been related to a fulminating pneumonia. In almost all cases pneumonia was the result of severe multiple lobe *Staphyloccocus* infection. In one instance it appears that death was due directly to interstitial pneumonia resulting from influenza virus infection.

Epidemiology

A brief discussion of the epidemiology of the disease is indicated. The experience accumulated to date indicates that epidemics in communities last from four to six weeks. In the Orient the attack rate was from 10 to 20 per cent of the community at large. In special groups — that is, in ship's crews, military recruits, and civilian camps and schools—an attack rate as high as 70 per cent has been noted. In the United States it was first thought that the disease was not highly contagious, since relatively little intra-familial spread took place. Apparently in the summer season contact is insufficient to result in rapid spread under our usual living conditions. When with fall and winter crowding occurs in closed spaces, spread appears to take place rapidly.

Laboratory Studies

Laboratory work involving influenza viruses is relatively simple. Isolation is carried out in embryonated eggs. In regard to this matter the United States was able to take advantage of the fact that its troops were stationed in many parts of the world. Asian influenza virus was isolated very early in the course of the outbreak in the Orient by the 406th General Medical Laboratory stationed in Japan. The virus was sent to the Walter Reed Army Research Institute for final identification. As noted earlier, the virus is quite different in its antigenic composition from immediate predecessors. Furthermore, while isolation was easy, the serologic problems relating to the complement fixation tests and the hemagglutination inhibition test proved to be more difficult than had been noted in A prime strains.

Possibly a word relative to the hemagglutination inhibition test is indicated. Influenza virus is one which has the ability to clump the red blood cells of certain mammalian species, including the chicken. In the presence of antibody to specific influenza virus clumping is inhibited. Using this technique, antibody can be demonstrated by determining to what degree

clumping of chicken red blood cells in the presence of influenza virus is inhibited. The test is called the hemagglutination inhibition reaction and is most useful in determining the presence of influenza antibody. Many serum specimens, however, contain nonspecific inhibitors which interfere with this reaction. Two specimens, "early" and "late," must be submitted to determine if a rise in antibody titer has occurred.

Diagnostic testing of individual patients becomes impossible when large numbers of people are ill. Even if there were sufficient funds, there would not be sufficient personnel to carry on large scale testing of specimens from everyone having an influenza-like illness. For this reason, and since identification cannot be used as a guide to treatment, it has been suggested that 6 to 12 specimens for diagnostic study be submitted from each locality reporting an outbreak. For serologic study 6 to 12 specimens should be submitted from patients early in the course of each patient's illness. Ten to 14 days later the second specimen should be obtained from each patient so that it can be determined whether a rise in antibody titer has occurred. Virus isolation studies may also be done. The latter is considerably more complicated than that necessary for serologic confirmation of infection. The patient gargles approximately 15 cc. of sterile broth, distilled water or saline, three times. If the gargled material is to be stored or transported a considerable distance, it should be placed under dry ice refrigeration. If the storage is only a matter of hours, ordinary ice refrigeration is sufficient. After the addition of penicillin and streptomycin, the gargled material is inoculated into the allantoic space of 11-day old embryonated hen's eggs. Allantoic fluid is harvested two days later. Ability of the allantoic fluid to cause clumping of chicken red blood cells establishes the presence of virus.

Vaccine

The Asian influenza virus was transmitted to six manufacturing drug houses on May 22, 1957, by the Public Health Service. The drug houses were well equipped to produce influenza vaccine rapidly, since manufacturers have been producing influenza vaccine for 14 years. The earliest releases of vaccine occurred on August 12. As of October 1, 1957, approximately 13.5 million cc. had been released.

Influenza vaccine has a rather interesting history. The very first vaccine which became available in 1941 appeared to be effective in approximately 70 per cent of the individuals inoculated. In 1947 it was found that the vaccine was no longer effective owing to the presence of a new type of influenza A virus which we have since come to know as the A prime strain. New strains have been major problems in protection against influenza. Possible mutation of influenza viruses makes it less likely that any vaccine from the past will be highly effective against a new strain. In the present situation, however, we have a very special field for investigation and study. The isolation of the virus in the Orient and the prompt beginning of manufacture of vaccine has made it possible to immunize a proportion of the population before exposure to the new agent. This is the first time it has been possible to inoculate against the "epidemic" strain before an epidemic occurred.

Related problems

There have been problems around vaccine, however. At first, it appeared that this virus did not grow as well in eggs as did earlier strains and that relatively small amounts of vaccine could be harvested from each egg. The situation has improved on repeated egg passage. Now six or seven doses of vaccine may be obtained from each egg. The supply of eggs in itself has been a matter of some concern. Earlier, approximately 50,000 eggs per week were used in the production of routine vaccines. At the present time about one million eggs per week are being used. Arrangements have been made between the biologics houses and the producers of embryonated hen's eggs, so that we may expect no shortage of eggs.

The concentration of influenza virus in the vaccine has been a matter of discussion. The advisers to the Military and Public Health Services have agreed on a concentration of 200 chicken cell agglutinating units per cubic centimeter of vaccine. (The chicken cell agglutinating unit is based upon the ability of the virus to clump chicken red cells, and it is used as a measure of virus concentration in the vaccine.) It should be stated, however, that the

Armed Forces prefer a vaccine of 500 units per cubic centimeter. Field trials have demonstrated that the rate of reactions is considerably higher when the more concentrated vaccine is used.

The question of dosage has likewise received considerable discussion. The committee advisory to the Public Health Service, which includes our Dr. Edward C. Curnen, has settled upon the following dosage schedule: 0.1 cc. will be given intracutaneously or subcutaneously to children from the age of 3 months up to the age of 5 years, and the dose will be repeated one to two weeks later. For children 5 to 12 years of age 0.5 cc. of the vaccine given subcutaneously is recommended. A second inoculation again will be given one to two weeks later. The recommended dose for age 13 and older is 1 cc. given once subcutaneously. After considerable controversy the Advisory Committee has again approved 1 cc. given subcutaneously for adults. It was recognized that antibody response to 0.1 cc. intradermally given in two doses, with an interval of a week or more, has in a few cases observed been approximately the same as that obtained from 1 cc. given subcutaneously. Large field trials carried out in the past 16 years used 1 cc. subcutaneously. It was decided not to depart from this dosage schedule since this was our only broad basis of reference for determining the effectiveness of influenza vaccine. The Armed Services intend to give 1 cc. doses of vaccine subcutaneously and to repeat the 1 cc. dose using the same route one month later. Reactions to the vaccine have been relatively mild. With the subcutaneous route approximately one half of the persons may be expected to develop soreness locally. A somewhat smaller number will note pain of the entire limb. Approximately 15 per cent will show mild chills and a slight rise in temperature. It is worth noting that influenza vaccine cannot be made completely reaction free since the virus itself is a toxic substance. Vaccine should be withheld from persons who are allergic to eggs, chicken feathers, or chicken.

Use of the vaccine is of some interest. If one wishes to prevent immobilization of a community, vaccination should be aimed at the productive group and the various workers necessary to the life of the community. If, on the other hand, one primarily wishes to prevent death, using the experience of the last several outbreaks, vaccination programs should be aimed at the very young and the very old. We have little in the way of guide lines to establish where we should aim. Deaths seen so far have been largely in persons beyond 10 years of age and in the middle-aged group. If this is a guide to the future experience, vaccination should be directed towards persons in the teenage years and in the productive age group. In this one respect, the mortality has shown a similarity between this outbreak and the 1918-1919 outbreak.

The handling of the Salk and Asian Influenza vaccines offers an interesting contrast. In the former there were many controls: Federal purchase, controlled allocations, and priorities. No real controls are in force for the handling of the Asian influenza vaccine. Free enterprise in the usual trade channels provides no special consideration for the individual (including the physician), and no health or strategic economic priorities. There is only the gentlemen's agreement among the manufacturers to supply the states according to population. North Carolina gets 2.6 per cent of that for civilian use. The recommendations as to protection on the basis of national defense and community and family considerations have no force and are largely ignored. It is enlightening to have the contrasting experiences so close together. There have been instances of unhappiness with both plans.

North Carolina Experience

The North Carolina experience is, of course, of special interest to us. In late June and early July 39 persons returned to this state from the Grinnell, Iowa, meeting. So far as we can determine 13 of them became ill of influenza-like disease. The first cases were reported from Winston-Salem. Very early the State Board of Health Laboratory, which is equipped with a virus diagnostic set-up, was able to demonstrate infection with the Asian strain of influenza virus. Subsequently a number of small one-family outbreaks occurred in mid-July. Returnees from the Boy Scout Jamboree at Valley Forge also introduced the agent into the state. Some of the Scouts were shown to be infected by the Asian influenza virus strain.

Relatively little respiratory disease was seen in the month of August and early in September.

At the present time the State Board of Health is receiving information from local health departments relative to the estimates of cases of influenza-like disease occurring in each of the 101 health jurisdictions. Influenza-reporting, for reasons which are obvious to you, such as the fact that many diseases resembling each other occur in this group and that when large numbers occur physicians are too busy to report individual cases, has made reporting of cases ineffective. North Carolina, in keeping with modern trends and the practice in most states, does not report individual cases. We have asked our health officers, however, to estimate, based upon industrial absenteeism, absenteeism from schools, and a survey of the general practitioneers, internists, pediatricians and hospitals in the community, numbers of cases. At the present time we are receiving reports of approximately 2,000 influenza-like illnesses per week — 6,093 last week (first week in October). Two localized outbreaks have come to the attention of the State Board of Health. One of these, presently occurring in a State Teacher's College in Winston-Salem, has numbered approximately 100 persons. The second outbreak, occurring in a State Teacher's College in Durham, has shown some 200-300 persons ill in a population group of 1300. In both instances the disease has been mild. In the Durham outbreak specific infection has been demonstrated by the presence of antibody among those ill. To date, of 364 blood specimens examined from the entire state, 104 have shown the presence of measurable antibody to the Asian strain of influenza virus. Many, however, have not yet been confirmed by a subsequent rise in titer to this strain of virus. The level of antibody titer to this particular virus has not been striking.

Summary

In summarizing the present situation it should be pointed out that, though deaths have occurred, the disease generally has been mild. Facilities are available for laboratory confirmation. In treatment a calm attitude is needed. The use of antibiotics is generally contraindicated. The disease, should an attack rate of 10-20 per cent be seen, could seriously disorganize community function. This must be taken into consideration in civil defense preparation since protection against Asian influenza might be of very great importance. We have a special opportunity, the first presented in influenza history, to immunize a large proportion of the population against the specific agent producing the influenza currently being seen. To the private physician, influenza may mean a large patient load and pressures for hospitalization, use of antibiotics and use of vaccine — all which may be difficult to place in proper perspective. Indications to date, however, are that a large supply of the vaccine will be produced rapidly and—we hope—sharply reduce the incidence of the disease.

Although some of us may still persist in referring to women as the weaker sex, it is apparent that, at the present rate, the weak shall inherit the earth. It is truly a case of "the fragile male." Bond, J. O.: The Fragile Male, Geriatrics 12:489 (Aug.) 1957.

While total death rates have been declining steadily and comfortably over the past half century, rates for women have dropped at a progressively faster rate than have those for men. This has been most marked in the white population where male death rates have declined 50 per cent since 1900, contrasted with a 65 per cent decrease for females, Bond, J. O.: The Fragile Male, Geriatrics 12:489 (Aug.) 1957.

A Study of Diffuse Cortical Atrophy of the Brain

ROBERT W. WILLETT, M.D.

RALEIGH

Diffuse cortical atrophy of the brain has been recognized more frequently in recent years mainly because of the increased use of pneumoencephalography in the diagnostic work-up of neurologic diseases. More information concerning the cause, symptomology, and natural history of this far from rare entity seems indicated. The past literature on the subject, though sparse, does contribute some interesting data. Diffuse degenerative changes in the cortex are known to occur with various types of vascular disease, chronic alcoholism, central nervous system infections, asphyxia, and certain birth and developmental conditions. The atrophy associated with repeated trauma to the head such as results from boxing, of course, is well known. Unilateral changes are not uncommonly the result of cerebrovascular accidents. Partial thrombosis of the internal carotid artery manifested clinically by progressive hemiparesis has been cited as the cause of generalized atrophy[1]. Presenile dementia (Pick's disease and Alzheimer's disease) is a rare cause of cerebral degeneration.

Fisher and Mann[2] studied a large group of patients whose presenting symptom was convulsive seizures beginning after the age of 30. One third of this group demonstrated by pneumoencephalogram some degree of atrophy, the cause of which was not obvious. No typical seizure pattern was evident, and no relationship was found between the amount of cortical wasting and the protein content of the spinal fluid. About half of the electroencephalograms done on these patients were reported as normal, and most of the remainder showed a generalized cerebral dysrhythmia without specific diagnostic features.

Another study of 20 adults with cortical atrophy of unknown cause was presented by Plum[3]. These patients had seizures, manifestations of corticospinal tract involvement, or both. Although mental dullness appeared later in some cases, the presence of atrophy did not necessarily imply early dementia. Jackson[4] reported convulsive seizures in 75 per cent of the patients he observed. Fleminger[5] recalled that seizures were the most common symptom recorded in his group.

The present study was designed to shed more light on this complex problem. Of especial concern and interest were: (a) the various causes, (b) the presenting signs and symptoms, (c) pertinent laboratory data including electroencephalograms, and (d) the natural course of the disease. The case material consists of 50 patients observed during the past five years who showed diffuse cortical atrophy by pneumoencephalogram. Thirty were seen at Duke Hospital and 20 were admitted to the Durham Veterans Administration Hospital. Only adults were included in the study. Patients ranged in age from 25 to 64 years, with the majority (31) falling in the 40 to 60 age group. Twenty-one had had symptoms for less than one year when first studied; 9 had been ill from 8 to 40 years.

Symptoms and Signs

The most frequent symptoms observed were those associated with changes in the mental status. Thirty-six patients showed some change in this sphere, although it was the presenting symptom in only 17. The most common complaints made by either the patient or relatives were forgetfulness and childish behavior associated with unstable mood. Other changes frequently mentioned were aggressive, agitated behavior, confusion, slow thinking, and disorientation; less frequently reported were depression, hallucinations, delusions, and anxiety.

The second most common symptom was that of convulsive seizures, which appeared in 33 patients and constituted the presenting symptom in 25, thus making it the most common initial complaint. The seizures were of the *grand mal* type in 18 patients, focal motor in 7, psychomotor in 3, atypical *grand mal* in 3, and both psychomotor and

Read before the Section on Neurology and Psychiatry, Medical Society of the State of North Carolina, Asheville, May 8, 1957.

Table 1

Symptoms of Cortical Atrophy

Symptom	No. Patients
Mental changes	36
Convulsive seizures*	33
Other neurologic complaints	24
Headaches	18

*Most frequent presenting complaint

grand mal in 2. There was nothing characteristic about these convulsions either as to type, onset, frequency, or duration.

Twenty-four patients had neurologic symptoms. A persistent unilateral hemiparesis, sensory disturbance, or both were noted in 16 of the 24. A more transient unilateral disturbance of a similar type, lasting from 15 minutes to several hours, was recorded by 4. Transient speech difficulties were noted by 4; permanent speech troubles were mentioned four times. Three patients had symptoms best described as generalized numbness, ataxia, and weakness. Three had transient episodes of diplopia, and 3 intermittent dimness of vision. Two complained of gross tremor and 1 of persistent dizziness.

A combination of seizures and mental symptoms was seen in 20 patients, seizures and neurologic changes in 15, and mental and neurologic abnormalities in 17. Only 10 patients had all three of the above symptoms. In addition to these, 18 had headaches of various types. These headaches were entirely dissimilar in location, type and severity, but not infrequently were a major complaint. The family history was noncontributory in all instances. Complicating disease processes included hypertension in 12 persons, diabetes in 2, pan-hypopituitarism in 1, lues in 1, and arteriosclerotic heart disease in 1.

Neurologic and Physical Findings

The neurologic examination on admission revealed definite abnormalities in 29 instances. Fifteen patients (a majority) showed hemisensory loss or hemiparesis. Five showed generalized spasticity and 1 generalized ataxia. Cranial nerve disturbances and visual field defects were present in 4 others. Twelve patients were found to be hypertensive and 18 showed definite evidence of widespread arteriosclerosis. Cardiomegaly was found by chest film in 5.

Table 2

Pneumoencephalographic Pictures in Cortical Atrophy

Outstanding Defect by Pneumoencephalogram	No. Patients
1. Ventricles enlarged on both sides with generally increased subarachnoid air	10
2. Ventricles normal but definite increase in subarachnoid air, generalized	9
3. Increased air over one cerebral cortex	8
4. Ventricle on one side larger than its opposite	7
5. Frontal atrophy with increased subarachnoid air	5
6. Both ventricles enlarged	5
7. Frontal atrophy with enlarged anterior horns	4
8. Para-saggital atrophy	2

Accessory Findings

Laboratory data

Laboratory studies were of interest in that only 1 of 49 serologic tests for syphylis was positive. Blood sugar values were found to be normal in 18 patients, high in 2, and 53 per 100 cc. in 1. Lumbar puncture was performed 47 times. In the majority of cases all findings were within normal limits. Cerebrospinal fluid protein values were normal except in 15 cases where the levels ranged between 55 and 82 per 100 cc. The initial pressure was normal except in 2 cases where the recordings were 230 and 420 mm. of water. Blood cell counts were abnormal in only 2 cases; one examination showed 13 polymorphonuclears, and another 160 crenated red blood cells.

Skull films and pneumoencephalograms

Skull films were interpreted as being within normal limits in 44 cases. Old fractures were found in 3 instances. Hyperostosis frontalis was diagnosed once, and bird shot was demonstrated outside the cranial cavity in 1 patient.

Pneumoencephalograms were performed on all patients. All showed evidence of generalized atrophy, but certain areas were particularly involved in some patients and the changes were not always absolutely symmetrical. In certain instances the ventricles failed to fill and abnormal amounts of air were observed only in the subarachnoid spaces. In others the excessive air filling was seen only in the ventricles (fig. 1). Table 2 shows the various pneumoencephalographic pictures and the number of patients demonstrating each type. Some degree of frontal atrophy was present in 13 instances. Arteriograms were done in 4 patients, including those with transient neuro-

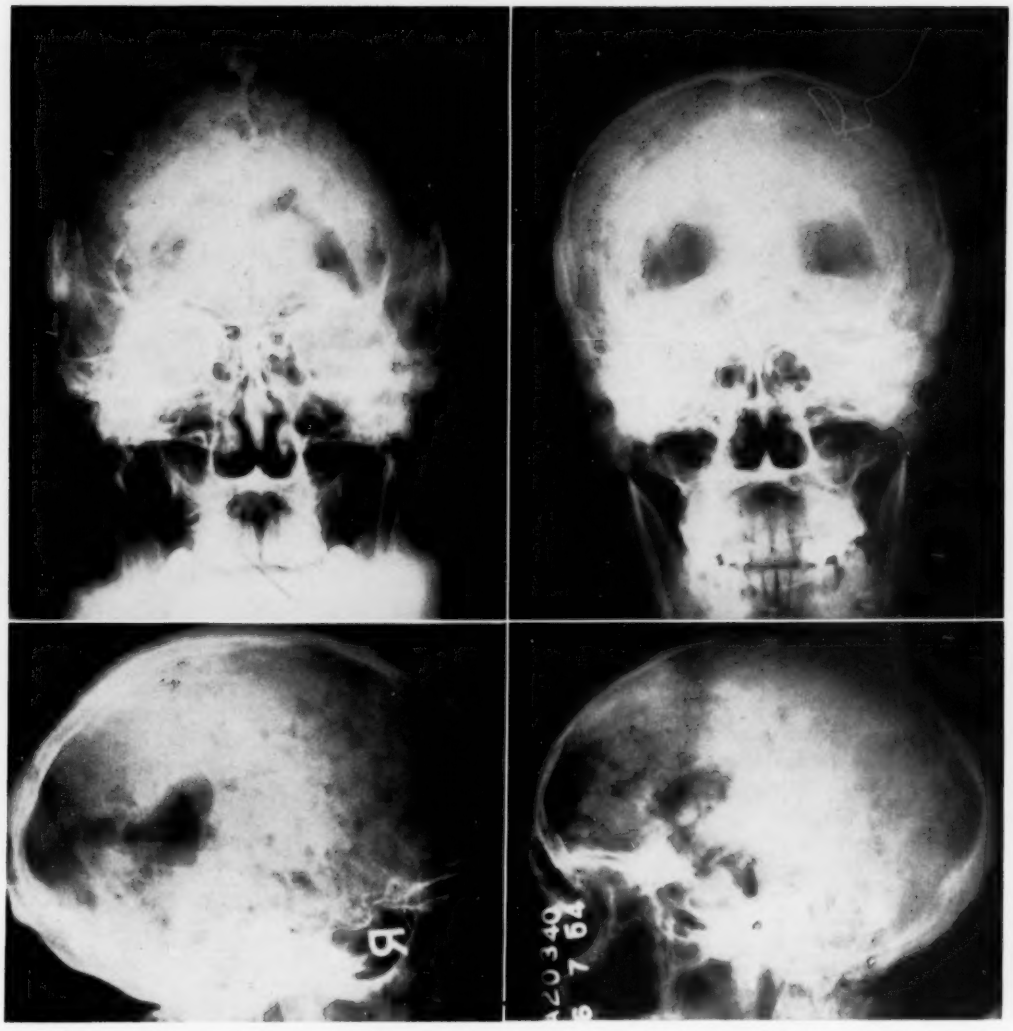

Fig. 1. Air patterns of atrophy. A. Para-saggital atrophy. B. Ventricular dilatation. C. Focal pockets of subarachnoid air. D. Marked frontal wasting.

logic signs, but no vascular lesions were demonstrated.

Electroencephalograms

Out of 46 electroencephalograms taken, 16 were found to be within normal limits. Of those which were abnormal, there emerged no uniform pattern suggestive of cortical atrophy. Seventeen patients showed either a generalized dysrhythmia with a predominance of slow waves, or a diffusely irregular pattern without change in amplitude. In 6 of these the abnormality was more prominent on one side. Bursts of generalized slow wave activity were observed in 4 instances. A focal disturbance with increased amplitude was located in the temporoparietal region in 6 cases and in the occipital area in 2 (fig. 2).

Generalized paroxysmal bilateral delta and theta waves with a frequency of 1 to 6 per second were seen in one instance of a large hemorrhage above the pons. There was no relationship between cases showing a focal electroencephalogram and a pneumoencephalogram with the abnormality predominating on one side. There seemed to be no relationship between the EEG and the clinical type of the illness; patients with

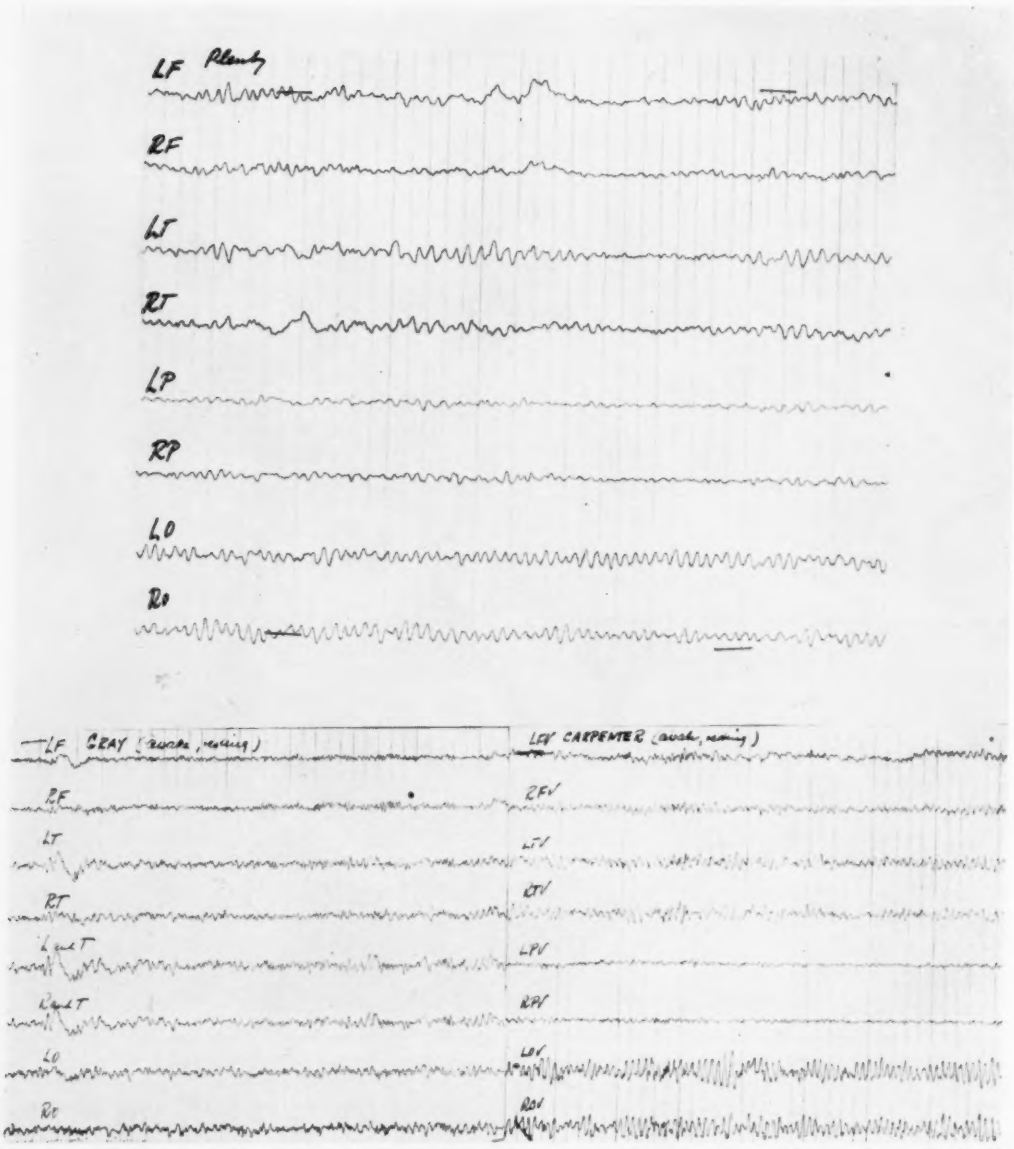

Fig. 2: EEG tracings in atrophy. A. Generalized slow waves, irregular form and normal amplitude. B. Slow waves, enlarged amplitude, left temporal focus. C. Slight generalized dysrhythmia.

tracing as were those who were seizure free.

Possible Causative Factors

An attempt was made to determine from the chart what factors could be incriminated as having contributed to the generalized atrophy of the cortex. In many cases multiple etiologic factors were present, making it impossible to determine the most important one in any specific case. Chronic alcoholism and a history of repeated head trauma were frequently associated in the same individual. Vascular disease was thought to play a prominent role in 18 instances. Evidence for vascular disease included significant hypertension, a past history of strokes, diabetes with advanced vascular disease, or a history of intermittent neurologic changes. Chronic alcoholism

Table 3

Possible Etiologic Factors in Cortical Atrophy

Possible Etiologic Factors	Times Implicated
Vascular disease	18
Chronic alcoholism	14
Head trauma	13
Unknown*	14
Hypoglycemia	2
Repeated convulsions	1
Meningitis	1
Generalized syphilis	1
Probable birth injury	1
Head surgery	1

*Four with generalized arteriosclerosis; 5 over 55 years old.

possibly played a part in 14 instances, and a history of severe head trauma was obtained in 13. No obvious causative condition could be uncovered in 14 patients. Of these, 4 had evidence of widespread arteriosclerosis with arteriosclerotic changes in the fundi, and 5 others were over 55 years of age. Repeated attacks of hypoglycemia were perhaps of importance twice —once in a diabetic on insulin and once in a patient with pan-hypopituitarism. In one instance the atrophy seemed related to idiopathic epilepsy and repeated seizures over many years. Other possible causative factors present in 1 patient each were meningitis, generalized syphilis, probably birth injury, and head surgery (table 3). The only difference in the patients from Duke Hospital and the Veteran's Hospital was the increased number of chronic alcoholics associated with repeated head trauma observed in the latter institution.

Postmortem examinations were done on 3 of these patients. In 1 a large hemorrhage of the mid-brain was found; in 2 generalized cerebral arteriosclerosis with encephalomalacia was evident.

Comment

The largest single group of patients with cortical atrophy fall in the 40 to 60 year age group and show definite evidence of degenerative vascular disease of the brain. Many of these patients had in their history episodes suggestive of strokes or transient periods of cortical ischemia. It is known that a single stroke is followed by a marked drop in the cerebral blood flow[5]. This drop cannot be explained by the infarct alone, and is thought to be due to the diffuse cerebral arteriosclerosis which precedes the vascular accident. Cerebral blood flow is even further reduced in patients with more chronic cerebral vascular disease, and in this group the cerebral oxygen consumption is also low. It seems likely that the atrophy found in those patients showing obvious signs of cerebral vascular insufficiency is the result of a reduction in the blood supply secondary to the narrowing and occlusion of the smaller cerebral vessels. Although diffuse atrophy has been reported with partial occlusion of the internal carotid arteries, no case of this type was discovered in the current series.

An explanation similar to that presented above may also hold for some of the 14 patients in whom no obvious cause for the atrophy could be found. Four of these people had definite evidence of generalized arteriosclerosis, and another 5 were over 55 years of age; in none were there signs of localized disease. Baker[6] has demonstrated certain hyalin and fibrotic changes occurring in the walls of the small cerebral arteries with age. In a study by Heyman and associates[5] of a group of persons over 45 years of age showing no evidence of cerebral vascular disease, a drop was observed in the cerebral blood flow and an increase in the cerebral vascular resistance. They believed this change to be "caused by a moderate degree of arteriosclerosis insufficient to alter cerebral function to the point of overt manifestation." Brody[7] has found a marked decrease in the neuronal density of the cerebral cortex with advancing age. It seems justified to wonder if in the present study some of the atrophies classified as of unknown etiology might also be explained on a vascular basis without showing localizing signs. Of course the decreased cerebral blood flow and increased vascular resistance might also be secondary to a loss of neurons dying from "old age," with resulting decrease in metabolic requirements. In this instance the circulatory changes would follow rather than cause the metabolic slow-down. Although many patients in this study had hypertension, this factor alone will not alter the cerebral blood flow[8]. Only 4 case histories out of the entire group were the least suggestive of the classic clinical picture of either Pick's or Alzheimer's disease, characterized by progressive dementia and speech difficulty.

Scheinberg[9] has demonstrated a definite

relationship between the mental status of patients with chronic cerebral vascular disease and the cerebral metabolic rate. Patients having vascular disease but showing no mental changes had a lower cerebral blood flow than normal, but the cerebral oxygen utilization was normal. Those with mental changes had a marked decline in both cerebral blood flow and utilization of oxygen, indicating that by the time mental changes occur the process of vascular disease is diffuse. It is of interest that the largest single complaint of the current group of patients was related to changes in the mental status.

Since recurrent head trauma plays such a prominent role in the development of brain atrophy, it would have followed that head injury due to the oft repeated convulsions of idiopathic epilepsy would have appeared more than once among the causative factors. One reason for this apparent discrepancy might be that pneumoencephalograms are seldom done on patients who have had idiopathic epilepsy for many years.

The cause of the diffuse brain atrophy seen so frequently in alcoholics did not become evident in this study. Whether this association is due to a direct toxic effect on the brain or is secondary to frequent head trauma is not clear. Repeated bouts of hypoglycemia are known to produce degenerative changes in nervous tissue. A low blood sugar level was possibly a contributing factor in 2 patients—1 a diabetic with frequently repeated insulin reactions, another a patient with pan-hypopituitarism and a low blood sugar.

The absence of a typical electroencephalographic picture substantiates the observations of previous workers. In the series reported by Levin and Greenblatt[10] a predominance of slow wave tracings were noted, and all patients with convulsive seizures were found to have some brain wave abnormality. In the present series the abnormal EEG patterns were equally nonspecific; however, patients with seizures not infrequently had perfectly normal records. The same authors reported a higher incidence of abnormal tracings among patients showing marked atrophy; such a relationship was not demonstrated in the current group of cases. Although some records revealed focal disturbances, there seemed to be no correlation between this finding and the presence of unilateral neurologic signs, jacksonian-type seizures, or pneumoencephalograms showing asymmetrical atrophy.

The prognosis depended upon the etiology. In most instances the course was intermittently but progressively dowhill, although some individuals recovered from an acute bout of symptoms. Progressive mental deterioration was not necessarily the rule.

Summary

Charts of 50 patients with a diagnosis of diffuse cortical atrophy proven by pneumoencephalograms were reviewed for the purpose of determining more about the causative factors, symptomatology, and natural history of this far from rare disorder.

Most of the patients fell in the 40 to 60 year age group. The most common symptoms were mental changes, convulsive seizures, and neurologic abnormalities. Seizures were of various types and were most often the presenting complaint. Hemisensory or motor losses were the most common neurologic sign.

The spinal fluid examination was usually normal except for an occasional slightly elevated protein content. Skull films rarely showed old fractures. The electroencephalogram was often normal, and, if abnormal, most frequently showed generalized dysrhythmia of a nonspecific type.

Causative factors most commonly encountered were vascular disease, alcoholism, and head trauma; more rarely encountered were hypoglycemia, meningitis, syphilis, birth injury, and head surgery.

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The Present Status of Ethyl Ether, Vinyl Ether and Ethyl Chloride in Anesthesia

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Since October 16, 1846, when William Morton gave the first public demonstration of ether anesthesia at the Massachusetts General Hospital in Boston, ether has continued to be the most widely used general anesthetic. Despite numerous attempts to supplant diethyl ether, the drug has remained the reliable standby of inhalation anesthesia. Although ethyl ether is a potent anesthetic agent, it possesses a wide margin of safety. All other inhalational agents must demonstrate some specific advantage over it in order to be selected for a given surgical or obstetric procedure. Since ether is the standard by which all new anesthetics are measured and thus has received extensive investigation, it will be considered in more detail than divinyl ether and ethyl chloride.

Many misconceptions about the pharmacologic actions and the physiologic effects of ether anesthesia still prevail in some modern textbooks of pharmacology. The purpose of this paper is to clarify many of these misconceptions.

Open drop ether anesthesia is often alluded to as the safest anesthetic. This is true only in the hands of the untrained anesthetist, a dangerous situation in itself. If this technique is used, oxygen should be insufflated under the mask via catheter at a rate of 1 to 2 liters per minute in order to maintain adequate oxygen concentrations. The carbon dioxide concentration under the mask remains around 1 per cent in the awake child, even though the oxygen flow is increased to 3 liters per minute (fig. 1). The absence of means to compensate respirations with this technique in order to maintain adequate alveolar ventilation is a definite disadvantage. The use of mineral oil or olive oil in the eyes to prevent conjunctivitis is erroneous, since the oil acts as a solvent for ether and prolongs its contact with the conjunctiva. Protection of the eyes with a rubber dam is beneficial.

Considerable nonsense has also been written about the harmful effects of impurities found in ether. Many anesthetic complications and deaths have been attributed to the presence of impurities rather than to improper administration. Traces of aldehydes or peroxides have no apparent harmful effect.

Read before the Section on Anesthesia, Medical Society of the State of North Carolina, Asheville, May 7, 1957.

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Ethyl Ether

Pharmacologic actions

The physiologic effects of ether anesthesia are the combined result of two pharmacologic actions—direct depression and reflex sympathoadrenal release. Thiopental aggrevates the direct depressant effect and suppresses the reflex sympathoadrenal effect. Curare significantly diminishes the output of epinephrine, presumably by inhibiting the response of the adrenal gland to its innervating cholinergic secretory fibers[1]. The reflex sympathoadrenal effects are more apparent during light anesthesia, while the direct depressant effects become manifested during deep anesthesia.

The administration of diethyl ether re-

EFFECT OF ADDITION OF O_2 UNDER OPEN DROP MASK ON INSPIRED CO_2 AND O_2 CONCENTRATIONS IN AWAKE CHILDREN

O_2 Flow L/min.	End-Inspired CO_2 %	Ave. Inspired O_2 %
0	1.1	20
1	1.0	28
2	1.0	38
3	0.9	42

Figure 1

sults in a reflex stimulation of the sympathetic nervous system and the adrenal medulla. This, in turn, results in the release of approximately 1 microgram per kilogram per minute of epinephrine and nor-epinephrine. The infusion of this amount of epinephrine and nor-epinephrine will reproduce many of the physiologic effects of ethyl ether anesthesia. There is available ample evidence of the difference in the circulatory effects of epinephrine and nor-epinephrine. When mixtures containing equal proportions of the two sympathomimetic amines are infused, the epinephrine effects apparently predominate. Some of the physiologic effects of nor-epinephrine are counteracted by smaller amounts of epinephrine.

Autonomic cardiovascular reflexes: Autonomic cardiovascular reflex disturbances may be initiated by nonphysiologic stimuli during the course of surgery. The sensory and motor elements of the somatic nervous system are depressed during general anesthesia. The function of the autonomic nervous system remains active, however, until profound metabolic depression is produced. Burstein and Rovenstine[2] attributed the celiac plexus reflex to increased tone of the splanchnic sympathetic nerves resulting from atropine administration, ether anesthesia, and stimulation in the region of the celiac ganglion during upper abdominal surgery, to produce a reflex in pulse pressure. There is a marked fall in systolic pressure, with relatively little change in the diastolic pressure or pulse rate (fig. 2). The reflex is intensified by administration of atropine but alleviated by vasopressors. The carotid sinus reflex, which is parasympathetic in nature and manifested by hypotension and bradycardia, is inhibited by the administration of atropine and ether anesthesia (fig. 3). Some believe that deep anesthesia is essential to abolish these cardiovascular reflexes during surgery. However, extensive personal experience with ethyl ether analgesia for cardiac surgery

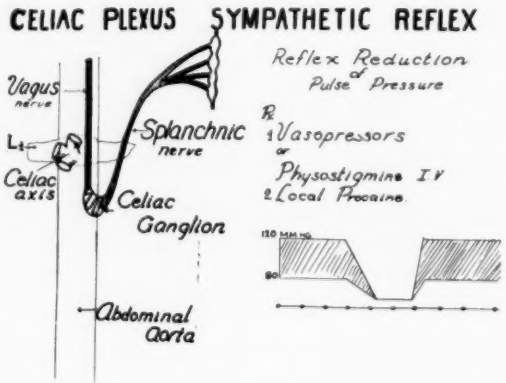

Figure 2

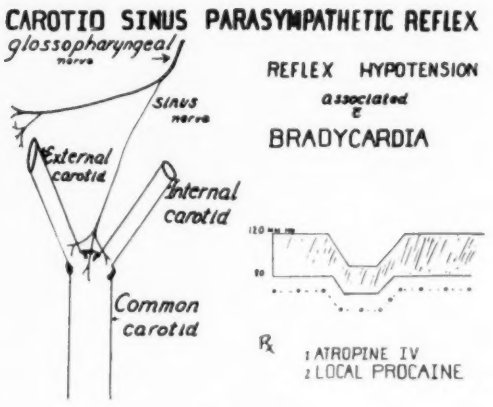

Figure 3

reveals a remarkable absence of deleterious reflexes. Ether analgesia does not depress the homeostatic sino-aortic mechanism and thus permits normal compensatory adjustment, while deeper anesthesia often abolishes this compensatory mechanism (table 1).

Effects on the central nervous system

Neurophysiologic studies of the anesthetic state have recently received great impetus from the investigative work of French, Verzeano, and Magoun[3]. These studies strongly suggest that the modification of neural transmission through the ascending reticular system is of major importance in the production of the anesthetic state. They have demonstrated that ether anesthesia blocks impulses conducted corticopetally through the reticular system, while the lateral sensory pathways continued to conduct with unimpaired intensity. This differential block is attributed to the multisynaptic formation of the medially placed reticular pathway as contrasted to the paucisynaptic lateral brain stem pathways.

The studies further demonstrated that lesions in the ascending reticular system produced slow patterns on the electrocephalogram typical of sleep or anesthesia, while stimulation of this area produced desynchronization manifested by a fast activity on the electroencephalogram. Thus it is suggested that ether analgesia is primarily stimulating to the reticular system and that the electroencephalographic pattern represents a desynchronization of the cortical activity. Artusio[4] has postulated that the

Table 1
Stage of Anesthesia

I. Plane
  1. Minimal amnesia—analgesia
  2. Moderate analgesia—complete amnesia
  3. Complete amnesia—analgesia
  Supplemented ether depth
  Unconsciousness
II. Delerium
III.
  1. Partial sensory loss
  2. (Complete sensory loss) Unsupplemented
  3. (Surgical relaxation) ether depth
  4. Intercostal paralysis
IV. Medullary paralysis

effect of diethyl ether is exerted in two places to block sensory impulses from reaching the cortex. During ether analgesia there is a block of the sensory fibers coursing laterally and a block at the cortical level without depression of the reticular system, which is manifested by the fast activity on the electroencephalogram (fig. 4A). Increasing the concentration of ether to produce anesthesia results in depression of the reticular system, which is manifested by the slow activity on the electroencephalogram (fig. 4B).

Cerebrospinal fluid pressure: Ether dilates the meningeal and cerebral vessels, but there is no significant increase in cerebrospinal fluid pressure as was formerly thought[5]. The increase in cerebrospinal fluid pressure associated with ether is usually the result of a rough induction, with straining, coughing, breath-holding, laryngospasm, bronchospasm, and upper respiratory obstruction. A bucking response during endotracheal intubation and hypoventilation, with associated hypoxia and hypercarbia, invariably produces considerable increases in cerebrospinal fluid pressure. It is now realized that a smooth induction and the maintenance of adequate alveolar ventilation does not produce a significant rise in the fluid pressure during ether anesthesia.

Neuromuscular blockade: Gross and Cullen[6] have demonstrated that ether anesthesia reduces the response of skeletal muscle to intra-arterial injection of acetylcholine and electrical stimulation of the nerve. This curariform effect is antagonized by neostigmine. Clinically, the synergistic effect of curare and ether at the motor end-plate is apparent, and smaller doses of curare can be used to produce muscular relaxation during anesthesia with ether than

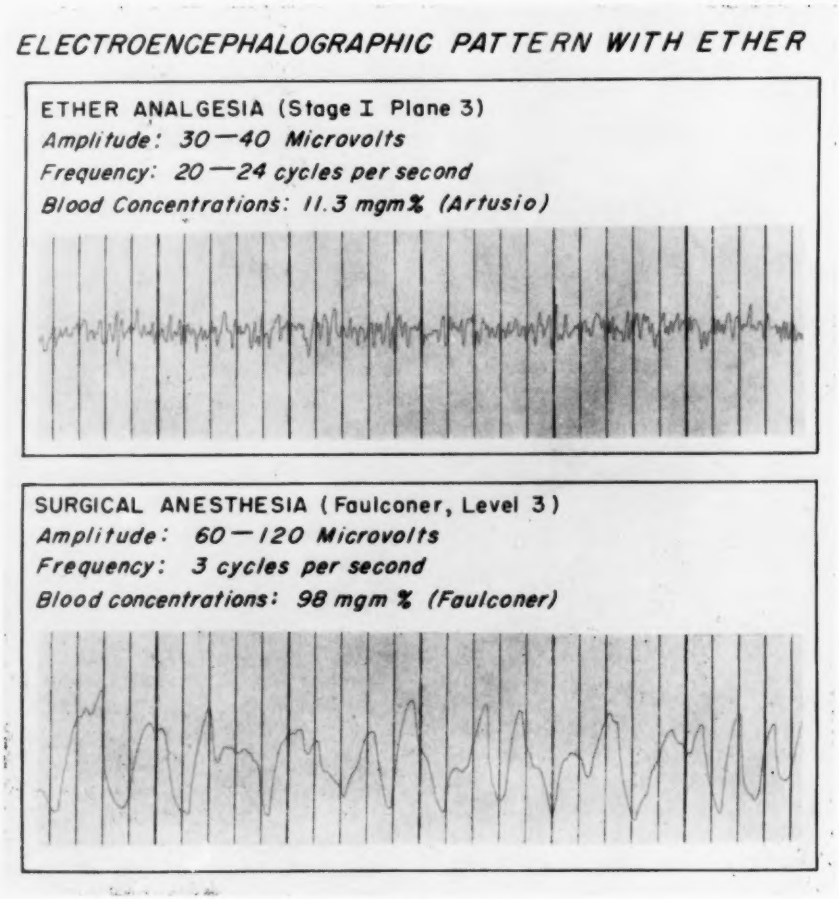
ELECTROENCEPHALOGRAPHIC PATTERN WITH ETHER
ETHER ANALGESIA (Stage I Plane 3)
Amplitude: 30—40 Microvolts
Frequency: 20—24 cycles per second
Blood Concentrations: 11.3 mgm% (Artusio)
SURGICAL ANESTHESIA (Faulconer, Level 3)
Amplitude: 60—120 Microvolts
Frequency: 3 cycles per second
Blood concentrations: 98 mgm % (Faulconer)

Figure 4A and B

with other agents. The neuromuscular blockade produced by decamethonium and succinylcholine is not enhanced by ether. This suggests that the action of curare and ether at the neuromuscular junction is similar. Recent investigation, however, has produced some evidence that the two types of blockade are not identical[7].

Convulsions: Certain factors usually contribute to the so-called ether convulsions. These factors are toxicity in a child who has been premedicated with atropine and anesthetized with ether in the presence of a high endogenous and exogenous temperature. This leads to an elevation of the metabolic rate, producing a high output of carbon dioxide which is inadequately eliminated and a high oxygen demand which is inadequately supplied. Thus the stage is set for a convulsion.

A neuromuscular phenomenon characterized by abnormal motor movements has been observed in association with divinyl ether which is the result of stimulation of the subcortical and spinal motor centers. In dogs this is manifested by a so-called running movement which disappears if the drug is discontinued immediately and 100 per cent oxygen is administered.

Effects on the respiratory system

Ether exerts on the medullary respiratory center a dual action consisting of direct depression and reflex stimulation. The predominance of one effect over the other is determined by the depth of anesthesia. The reflex stimulation of the respiratory center is due largely to the stimulating effect of mobilized epinephrine, the sensitization of pulmonary stretch receptors, and the stimulation of extrapulmonary sensory re-

ceptors[8]. The development of metabolic acidosis will also produce reflex stimulation of the respiratory center through the chemoreceptors of the carotid and aortic bodies. The final effect on alveolar ventilation is the result of the interaction of reflex stimulation and direct depression of the respiratory center, together with the alterations produced on neuromuscular conduction and the reactivity of the respiratory muscles.

The salivary and mucous glands are stimulated during induction and depressed during maintenance. The secretions develop mostly in the upper respiratory tract where the salivary and mucous glands are more abundant. Premedication with anticholinergic drugs and induction with thiobarbiturates will reduce this secretory activity.

Frequently reference is incorrectly made to the irritating actions of ether on the lungs. No cytologic changes can be demonstrated in the mucous membranes of the bronchioles or alveoli following ether anesthesia. Pulmonary edema, pneumonitis, or the activation of latent tuberculosis is not due to a direct effect of ether.

Ether is a bronchodilator and is thus a beneficial anesthetic agent for the patient with bronchial asthma. The bronchodilatation results from the combined effect of direct depression of smooth muscle and to reflex sympatoadrenal release.

Central cardiac effects

In 1927, Blalock[9] demonstrated that ether anesthesia in the dog is associated with an increase cardiac output. From further studies he concluded that the increased cardiac output was due to a direct myocardial stimulation by ether[10]. This incorrect interpretation has remained unchallenged until recently. Fisher and his associates[11], in 1951, demonstrated that ether acts as a direct myocardial depressant in the heart-lung preparations of dogs. Brewster and Issacs[2], in 1953, discovered that the increased cardiac output in the dog was due to the reflex release of nor-epinephrine and epinephrine.

Thus the safety of the action of ether upon the myocardium is determined by the quantitative reflex release of epinephrine and nor-epinephrine from the adrenal medulla and sympathetic nerve endings, which by virtue of their positive inotropic effect upon the myocardium antagonize the direct myocardial depression or negative inotropic effect of diethyl ether.

The clinical significance of this myocardial effect is that critical myocardial depression associated with profound hypotension may result from the direct depressant effect of diethyl ether upon the myocardium of a patient in whom the reflex release of epinephrine and nor-epinephrine from the adrenal medulla and sympathetic nerve endings is reduced or abolished.

The danger of critical myocardial depression during ether anesthesia is present in the following situations:

1. Drugs
   a. Antihypertensive therapy with veratrum alkaloids, Rauwolfia preparations, hydralazine, and hexamethonium
   b. Chlorpromazine
2. Spinal anesthesia supplemented with ether when sympathetic blockade is still present.
3. Surgical adrenalectomy or thoracolumbar sympathectomy
4. Pathologic hypofunction of the adrenal medulla
   a. Addison's disease
   b. Cushing's syndrome
   c. Adrenogenital syndrome
5. Subnormal sympathoadrenal release
6. Decreased response of a diseased myocardium to the positive inotropic effect of epinephrine.

During induction the cardiac rate is increased mainly because of the release of epinephrine. Ether does not sensitize the cardiac conducting tissue to epinephrine and related sympathomimetic amines. Spontaneous arrythmias are uncommon during ether anesthesia when adequate alveolar ventilation is maintained. When they do occur, they are supraventricular in origin. Continuous electrocardiographic recording during ether analgesia for cardiac surgery has not revealed any myocardial irritability except during direct cardiac manipulation.

Peripherovascular effects

Two mechanisms are involved in the pheripheral vasodilatation produced by ether: (1) depression of the vasomotor center, and (2) direct depression of the smooth muscle of the blood vessels. Hershey

and Zweifach[13] have shown that during hemorrhage ether predisposed the peripheral vascular compensatory mechanisms to early and extensive deterioration, decreased the tolerance to hemorrhage, diminished the response to blood transfusion, and modified the peripheral vascular reactivity to vasoconstrictor drugs.

Effects on the blood

The hemoconcentration observed during ether anesthesia is due to the combined effects of a reduction in plasma volume and the reflex sympathetic effect of splenic contraction. There is an increase in the flow of lymph which is probably indicative of the transfer of fluid from vascular to extravascular compartments.

Effects on the gastrointestinal system

Gastrointestinal tone, motility, and secretory activity are diminshed or completely inhibited during ether anesthesia. This is due to the direct depression of the smooth muscle of the gastrointestinal tract and reflex sympathoadrenal release.

The high incidence of nausea and vomiting attributed to ether anesthesia by both the layman and medical profession has been unfounded. Often this is chiefly due to faulty and improper administration of the agent, hypoxia during or following operation, the operative procedure, and narcotic drugs used for premedication or postoperative pain relief. Waters[14], in 1936, reported an incidence of 57 per cent with ether. Stephen[15], in 1954, using modern anesthetic techniques to administer ether, reported an incidence of 38.5 per cent without Marezine, and 25.8 per cent with Marezine. A study of nausea and vomiting in patients undergoing cardiac surgery with hypnotic doses of thiopental for induction and analgesic concentrations of ether for maintenance revealed an incidence of 4.2 per cent (table 2).

Table 2
Comparative Incidence of Postoperative Vomiting with Ether

	Per Cent
Waters (1936)	57
Stephen (1954)	38.5
Stephen (1954) with marezine	25.8
Ether analgesia for cardiac surgery	4.2

Metabolic effects

As a result of the improvements in anesthetic techniques and biochemical investigation, many of the older views concerning the metabolic effects of ether need modification. Also, much of the biochemical investigation of the metabolic effects of ether were done in animals and the results are not always transferable to man. The reflex sympathoadrenal stimulus by diethyl ether anesthesia produced hyperglycemia by glycogenolysis. If the nerves to the suprarenal glands are blocked by spinal or epidural anesthesia, hyperglycemia and metabolic acidosis are not produced. Thus the metabolic acidosis is also secondary to reflex sympathoadrenal release[16]. Pentobarbital and thiopental also inhibit the production of hyperglycemia by ether[17].

Disturbances in acid-base equilibrium are usually due to alterations in ventilation. In the adult human, the proper administration of ether with adequate alveolar ventilation does not cause metabolic acidosis[18]. In most infants and many children, however, a moderate degree of metabolic acidosis develops largely because of an increase in the blood lactic acid[19].

Thus a modification in our attitude toward the administration of ether to the diabetic patient is required. All that is really necessary in the management of the diabetic patient during surgery is to administer adequate insulin and glucose to maintain carbohydrate metabolism without producing hypoglycemia. The type of anesthetic agent used is far less important than its proper administration.

Liver function: There is a transient depression of liver function and the secretion of bile and bile salts during ether anesthesia. Clinical experience, however, seems to indicate that anesthesia *per se* when conducted with ether does not seriously influence the course of liver disease unless the exposure is excessive and is associated with hypoxemia. A well conducted anesthesia, with the maintenance of adequate tissue oxygenation and blood pressure, is more important than the effect of ether in preventing liver damage. The protective action of oxygen compares favorably with that of a high carbohydrate diet prior to anesthesia.

Effects on renal function

Ether anesthesia is accompanied by a suppression of urine formation and a compensatory polyuria during recovery. Fol-

lowing induction of anesthesia there is a marked reduction of the glomerular filtration rate, the effective renal plasma flow, and the output of water and electrolytes. The fall in filtration is usually less marked than that in effective renal plasma flow, so that the filtration fraction rises[20]. Since these alterations of renal function are associated with either no change or a slight increase in the arterial pressure, a marked intrarenal vasoconstriction must occur, presumably affecting both afferent and efferent arterioles. The output of water and electrolytes decreases more than the filtration, indicating a relative augmentation of tubular reabsorption. The increased tubular reabsorption is due to the stimulation of the supraoptic-hypophyseal system and the release of the anti-diuretic hormone from the posterior pituitary gland. These effects on renal function are not specific for ether anesthesia, but seem to be associated with the state of general anesthesia regardless of the anesthetic agent used. Although urinary output is temporarily suppressed, no specific cytologic changes can be demonstrated in the renal parenchyma. The effect is purely functional.

Effects on uterine activity

Ether inhibits uterine activity and in deep planes causes marked uterine muscular relaxation. It passes through the placenta to narcotize the fetus. When used to supplement the less potent anesthetic gases, ethylene and nitrous oxide, minimal concentrations can be used without producing the deleterious effects seen with ether alone.

Divinyl Ether

Divinyl ether is often referred to as a hybrid of ether and ethylene because chemically it is similar to both. It is four times as potent as diethyl ether. Induction and recovery are rapid, and the postoperative period is relatively free of nausea and vomiting. During induction the salivary and mucous glands are strongly stimulated. The production of copious secretions may prove troublesome if the patient has not been premedicated with atropine. Divinyl ether is also a bronchodilator. Repeated or prolonged administration produces necrosis of the liver of the central lobular type. This effect is enhanced by coexisting hypoxia. The eye signs are not reliable in assessing the depth of anesthesia. Eyeball activity may be active in the presence of good muscular relaxation.

Divinyl ether is useful to facilitate the induction of diethyl ether by the open drop technique and to fortify the analgesia of nitrous oxide and ethylene by the semiclosed method. It also can be used for minor surgical procedures, but should not be used longer than 30 minutes because of its hepatotoxic properties.

Ethyl Chloride

Ethyl chloride is a halogenated hydrocarbon with pharmacologic properties similar to chloroform. Its rapid, pleasant induction is the only feature which has sustained its popularity. Its safety margin is small, owing to its extreme potency and volatility. Initial vagal stimulation with bradycardia makes premedication with atropine essential. As anesthesia deepens, cardiac output is decreased by direct myocardial depression. Myocardial irritability is enhanced. The cardiac conducting tissue is sensitized to epinephrine and related sympathomimetic amines. Ventricular fibrillation may be produced by this combination. With many safer anesthetic agents available, its use as an inhalational anesthetic is not justified.

The use of ethyl chloride to produce local anesthetic effects by refrigeration has been unsatisfactory. Not only does destruction of healthy tissue sometimes occur, but pain is often experienced when the tissue is incised. As a local analgesic, ethyl chloride leaves much to be desired.

Balanced Pharmacologic Anesthesia

The anesthetic state can be broken down into three components: hypnosis, analgesia, and muscular relaxation. Drugs should be employed to produce each of these components for which their pharmacologic properties are primarily suited. Thus hypnosis can be accomplished with the thiobarbiturates, analgesia with ether, and muscular relaxation with the neuromuscular blocking agents. Attempts to produce these three components with ether alone will inevitably result in unnecessary depression of important physiologic mechanisms. Thus the administration of ether in analgesic concentrations, preceded by hypnotic doses of thiobarbiturates for induction and supplemented with a neuromuscular blocking

Table 3

Components of Supplemented Ether Anesthesia

Thiobarbiturates	——>	Hypnosis
Ether	——>	Analgesia
Muscle relaxants	——>	Relaxation

Equals anesthesia with few side effects

agent for muscular relaxation associated with the maintenance of adequate alveolar ventilation, will prevent many of the deleterious side effects seen with ether alone (table 3).

Conclusion

The judgment and skill of the anesthesiologist are more significant than the anesthetic agent employed. In the past too much emphasis has been placed on individual agents in trying to explain the etiology of anesthetic complications. A patent airway, adequate tissue oxygenation, and carbon dioxide elimination accompanied by the application of sound physiologic and pharmacologic principles are the basic underlying requirements in the management of any patient during anesthesia and surgery. With the advent of medical anesthesia associated with improved biochemical investigational methods and more extensive research in anesthesia, many of the untoward side effects attributed to ether and other agents have been shown to be directly related to faulty and improper administration. It is not the automobile that kills, but the man behind the wheel.

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In 1900, a boy baby born in the United State could look forward on the average of 46.3 years of life. A girl born that year could expect to live an average of two more years, or a total of 48.3 years. By 1954, largely because of the elimination of the deaths from infectious diseases in infancy and childhood, males could expect to live 66.8 years. However, a female child born in 1954 could expect to live 72.9 years, an expectancy of six more years than the male. Bond, J. O.: The Fragile Male, Geriatrics 12:489 (Aug.) 1957.

The Effect of Potassium Depletion on the Kidneys

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CHAPEL HILL

It has been known since 1937[1] that experimental potassium depletion in animals is frequently associated with anatomic lesions in the renal tubules, and during the last decade there have been a number of reports of renal tubular lesions in patients dying during or following a period of potassium deficiency[2]. Prior to 1953, however, little attention was paid to the possibility that potassium depletion in human beings might cause significant derangement of renal function, although there were occasional reports noting polyuria and polydipsia in such patients.

Reports from the Literature

In 1953[3] and 1956[2] Schwartz and Relman of Boston published their excellent studies with respect to renal function and histology in potassium-depleted patients. Table 1 summarizes some of their data. Potassium deficiency developed in patients nos. 1 and 5 as a result of chronic diarrhea. The second, third, and fourth patients were all women who had taken excessive amounts of laxatives for many years. The letter "A" refers to data obtained at the time the patients were known to be potassium-depleted; the letter "B" refers to studies done subsequent to potassium repletion. The interval between A and B is indicated in the second column. It will be noted that some but not all of these patients had albuminuria, some but not all had slight elevations of the blood urea nitrogen or nonprotein nitrogen, some but not all had abnormalities (usually slight) of the urinary sediment. All the patients had a significant impairment of urinary concentrating power. The phenol red excretion was measured in only 4 of the 5 cases, but in all these it was diminished. After potassium repletion, all the abnormalities returned to or toward normal, and in 4 of the 5 the interval was only two to three months. In cases 1 and 3, the authors obtained renal biopsies during potassium depletion and again after potassium repletion. Tubular lesions were evident at the time of potassium depletion and were thought to be mainly in the proximal convoluted tubules. The biopsies performed after repletion showed evidence of repair.

Table 2 contains some of the available data from the literature with respect to urinary findings and renal function in potassium-depleted patients[4]. This summary includes cases of potassium deficiency arising from various causes, and almost all are examples of probable rather than rigidly proved forms of this condition. Hypokalemia was present in all, and in the majority there was some likely cause for excessive loss of potassium from the body. It is important to point out, however, that factors other than potassium depletion could have contributed to renal abnormalities in all these cases, and hence they cannot be taken as conclusive evidence for the effect of potassium deficiency alone. Thus chronic diarrhea may have been associated with deficiencies of many factors in addition to potassium, and primary hyperaldosteronism is generally associated with significant hypertension. To a lesser degree, the same qualification applies to the 5 cases of Relman and Schwartz, and unfortunately the few studies of relatively pure experimental potassium depletion in humans which have been reported do not provide much data with respect to functional or anatomic effects on the kidney.

As in the cases of Relman and Schwartz[2,3], the most consistent abnormality in this random group of potassium-depleted patients is an impairment of the urinary concentrating mechanism, which was evident in all but one of those tested. Albuminuria was present in most but not all of the cases. The urinary sediment was abnormal (usually to a slight degree) in most but not all cases. The blood urea nitrogen or nonprotein nitrogen was elevated in some but by no means all of the cases, and was almost never extremely high.

Cases Studied at North Carolina Memorial Hospital

The last 4 cases represent patients with severe potassium depletion whom we have

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Table 1

Evidences of Renal Damage in Potassium Depletion and After Potassium Repletion*

Case	Interval (Months)	Albuminuria		Abnormal Urinary Sediment		B.U.N. Mg. per 100		Maxium Specific Gravity		15 Min. P.S.P. % Excreted		Glomerular Filtration Rate C-IN ml./min.		Effective Renal Plasma Flow C-PAH ml./min.	
	A—>B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
1	18 mos.	No	No	No	No	—	—	1.005	1.022	12	26	64	—	247	—
2	2 mos.	Yes	No	Yes	Slight	27	13	1.005	1.021	16	30	43	103	315	584
3	3 mos.	No	No	No	No	15	—	1.011	1.020	9	24	51	63	362	307
4	3 mos.	Yes	?	No	No	16	—	1.013	1.026	—	—	103	116	379	507
5	2 mos.	Yes	No	Slight	No	NPN =45	NPN =35	1.008	1.023	3	21	43	80	88	407

*From the data of Relman(2) and Schwartz(3).

had the opportunity to study at North Carolina Memorial Hospital. The first of these, N. P., was in her seventh month of pregnancy, and was acutely ill following 10 days of severe diarrhea. She was markedly anemic and weak. She had an extremely low serum potassium level, the full explanation of which was never established, although it was essentially certain that it was at least partly the result of large losses of potassium associated with the diarrhea. There were no excessive losses of potassium in the urine. She had a slightly abnormal urinary sediment, but this may have been due to a complicating urinary tract infection. There was no albuminuria. The blood urea nitrogen was 20 mg. per 100 cc. (definitely elevated for a pregnant woman), and this subsequently dropped to 6 mg. per 100 cc. after potassium repletion and delivery. The maximum urinary concentration was to a specific gravity of 1.005, and the 15-minute phenol red excretion was less tahn 5 per cent. The infant died *in utero*, but the patient survived and appeared to recover fully. Unfortunately it has never been possible to do follow-up renal function studies.

The second and third patients are both examples of chronic potassium depletion associated with excessive use of laxatives and are therefore similar to cases 2, 3 and 4 reported by Relman and Schwartz. The first of these, N. W., had an essentially normal urinary sediment except for occasional white cells, had no albuminuria, and had entirely normal renal function studies except for a markedly impaired ability to produce a concentrated urine. This patient was given large amounts of potassium over a week or more and has remained in apparent potassium balance for the intervening seven months. Her urinary concentrating ability was entirely normal when retested six months after potassium repletion. The third patient, S. V., had a trace of albuminuria and a slightly abnormal urinary sediment (again occasional white cells). The blood urea nitrogen was minimally elevated, and the urinary concentrating ability was definitely impaired. Several months after potassium repletion a random urinalysis showed a specific gravity of 1.016, and the blood urea nitrogen was normal.

The fourth patient, V. C., was admitted in a state of agitated disorientation. Her initial serum potassium level was extremely low. The cause of what was undoubtedly a profound state of potassium depletion proved to be a variant of Cushing's syndrome due to bilateral adrenal hyperplasia in which the predominant manifestations were the electrolyte disturbances and which was therefore thought to represent a predominantly aldosterone-secreting form of this condition. Again, the one impressive abnormality with respect to the kidneys was a marked impairment of the urinary concentrating mechanism. This was associated with variable degrees of polyuria, a symptom which was noted in many of the other case reports cited in tables 1 and 2. This patient had a bilateral adrenalectomy, and was finally able to maintain a normal serum level thereafter. Satisfactory follow-up studies were impossible, however, because a number of complications developed and she finally died with generalized cryptococcosis several months after adrenalectomy.

Table 2

EVIDENCES OF RENAL DAMAGE IN POTASSIUM DEPLETION

CASE	CAUSE OF K DEPLETION	SERUM K mEq./L	ALBUMINURIA	URINARY SEDIMENT	URINARY CONCENTRATING ABILITY	B.U.N OR N.P.N	P.S.P. EXCRETION
Williams and MacMahon (1947)	Chronic Diarrhea	2.9	Yes	Granular Casts	—	Elevated	—
Luft et al (1951)	Idiopathic (Adrenal adenoma)	2.9	Intermittent	Occasional Wbc and Rbc	Impaired 1.011	—	—
Luft et al (1951)	Idiopathic	2.0	No	Wbc and Rbc	—	Normal	—
Keye (1952)	Steatorrhea	<1.3	Yes	Rbc and Granular Casts	[1.000 on Admission]	Elevated	—
Wyngaarden et al (1954)	Excessive Urinary Losses – ? Cause	2.6	Yes	Many Rbc Occasional Casts	Impaired 1.011	Elevated	—
Evans and Milne (1954)	Aldosteronism	1.4	Yes	Occasional Rbc and Wbc	Impaired 1.011	Normal → Elevated	—
Mader and Iseri (1955)	Aldosteronism	1.6	Trace	Normal	Impaired 1.010	Normal	—
Foye and Feichtmeir (1955)	Aldosteronism	1.8	Trace	Normal	Impaired 1.009	Normal	—
Conn and Louis (1956)	Aldosteronism	1.6	Trace	Normal	Impaired 1.011	Normal	Normal
Holten and Petersen (1956)	Probably Aldosteronism	2.3	Yes	Occasional Rbc and Wbc	Impaired 1.018	Normal	—
Dustan, Corcoran and Page (1956)	Aldosteronism	2.8	Yes	Rbc Wbc	Impaired 1.016	[Normal C_M]	—
Ditto	Aldosteronism	2.4	Yes	Wbc	Impaired 1.013	[Normal C_M]	—
Ditto	Aldosteronism	1.8	Yes	Wbc	Impaired 1.011	[Normal C_M]	—
Fine et al (1957)	Aldosteronism	2.3	Trace	Occasional Wbc and Rbc	Normal 1.026	Elevated	—
N.P. N.C.M.H. #2-40-08	Diarrhea and Pregnancy	1.5	No	[Infection]	Impaired 1.005	Elevated	Impaired
N.W. N.C.M.H. #4-74-49	Chronic Laxatives	2.1	No	Occasional Wbc	Impaired 1.006	Normal	Normal
S.V. N.C.M.H. #3-46-54	Chronic Laxatives	1.9	Trace	Occasional Wbc	Impaired 1.010	Elevated	—
V.C. N.C.M.H. #2-53-39	Adrenal Hyperplasia	1.5	Trace	Few Wbc	Impaired 375 mOsm.	Normal	Normal

Table 3

Maximum Achievable Urinary Concentration of Potassium Depleted and Control Rats*

Duration of K-deficiency	Muscle K mM./100 Gm. f. f. s.		Concentration of Urine Milliosmolal	
Weeks	Control	K-deficiency	Control	K-deficiency
1	47.6	42.8	2550	2132
3	45.8	41.7	2545	1962
2	48.2	37.9	2636	1808
4	47.9	34.0	2516	1710
2-½	44.8	26.6	2491	990

*This table is based on data reported in more detail elsewhere

Studies of Potassium Depletion in the Rat

During the past several years a group of us in the Department of Medicine at the University of North Carolina has been studying the effect of experimental potassium depletion on the renal concentrating mechanism of the rat. These studies[5] represent the joint efforts of Dr. Robert Winters, Dr. Frank Williams, Dr. John Bradley, Dr. Louis Welt, and I. In addition, the kidneys of these rats have been studied histologically and by microdissection by Dr. Jean Oliver of the Renal Research Unit in Summit, New Jersey. Potassium depletion was achieved by a potassium-free intake and supplemental sodium bicarbonate. Control rats received the same basic diet but with adequate amounts of potassium. The ability to form a concentrated urine was tested by collecting urine following an injection of vasopressin-in-oil. In table 3 the maximal concentration of the urine achieved by various groups of rats is compared to the concentration of potassium in fat-free muscle solids. The latter is considered to be an index of the severity of potassium depletion.

A separate control group was tested with each experimental group, and the concentrating ability of control rats was readily reproducible. It will be noted that with increasing degrees of potassium depletion there was a progressive decrease in the maximum urinary concentration achieved. On the basis of additional data, it has been possible to conclude that this defect of the renal concentrating mechanism cannot be explained by a deficiency of any known factor other than potassium, that it is not simply the result of general nutritional failure, and that it is related to the total concentration that the kidney can achieve rather than to the concentration of any one particular urinary solute.

As will be reported in the near future by Dr. Jean Oliver, the most consistent anatomic lesion in the kidneys of these potassium-depleted rats is found in the collecting ducts. This appears to be a unique lesion and achieves added interest when considered in relation to the physiologic defect, since several recent lines of evidence suggest that at least part of the urinary concentrating mechanism is located in the collecting ducts.

Summary

There is now a substantial body of circumstantial evidence in human beings and experimental evidence in animals which implicates potassium depletion as a specific cause of functional and anatomic derangements of the kidney. The most consistent alteration of renal function in potassium-depleted patients appears to be an impairment of the capacity to produce a highly concentrated urine, although other functional abnormalities also occur. In rats, experimental potassium depletion leads to a progressive impairment of the renal concentrating mechanism and to what appears to be a unique anatomic lesion in the renal collecting ducts. It is possible that this collecting duct lesion and the impairment of the renal concentrating mechanism represent the primary effects of potassium depletion on the kidney, and that many or all of the other renal abnormalities which have been observed are subsequent and perhaps secondary developments.

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Thrombotic Thrombocytopenic Purpura

A Case and A Brief Review of the Literature

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GREENSBORO

The disease thrombotic thrombocytopenic purpura was first described by Moschovitz[1] in 1925, and given its name by Singer[2] in 1947. Its outstanding feature is the appearance of innumerable occlusions of small caliber arteries, arterioles, and capillaries by an amorphous or grandular acidophilic material[3]. The clinical manifestations form an unusual triad; thrombocytopenic purpura, hemolytic anemia, and transitory bizarre neurologic symptoms and signs. Owing to the increasing number of cases reported in the literature, this entity can no longer be regarded as a medical curiosity. The following case, diagnosed *in vivo*, is presented because it is so characteristic of this disease.

Case Report

A 28 year old housewife was admitted to Moses H. Cone Hospital on May 5, 1954, because of jaundice. The patient had noted mild discomfort in the epigastrium for about one week before the onset of her present illness. Twenty-four hours before admission she suddenly became extremely nauseated, vomited once, became anorexic, had a severe headache, and noticed that her eyes were yellow.

Past history

In July, 1953, she was kept in bed for three weeks because of infectious hepatitis. In early childhood she and a younger brother had had attacks of jaundice at the same time.

Sixteen months before admission she had been delivered of a normal healthy child. She was extremely nauseated and had frequent nosebleeds throughout the entire pregnancy, but no jaundice. She was kept on a salt free diet during the pregnancy, although she did not think that she had anything wrong with her kidneys or an elevation of blood pressure.

The patient worked at a retail store and had no contact with fumes or chemicals at her job. However, she had helped her father spray tobacco with some sort of chemical three days before the onset of her present illness. She did not recall any rats around her home, but she had a dog which had been placed in a veterinary hospital in December, 1953, with a diagnosis of pneumonia.

The history also revealed that the patient had had what was called "rabbit fever" on two occasions—once at the age of 18 years and again at 22. On each occasion she had broken out with skin lesions and had had some fever, but had not seen a physician. Dilatation and curettage had been done two or three years previously, and the pathologic report was negative. She was told five years before that she had pyuria, but there were no other gastrourinary symptoms. Her average weight was about 145 pounds, increasing up to 165 pounds since the birth of the baby. She had not used alcohol and had not been taking any form of medication recently. The only cleansing material she had used around the house was Ajax.

Physical examination

The patient was a well developed, well nourished, somewhat overweight young white woman who had definite icterus of the skin and sclerae and who appeared subacutely ill but was mentally alert. The temperature was 99.4 F., the pulse 80, weight 160 pounds, and blood pressure 134 systolic, 95 diastolic. There were four or five dime-sized contusions or purpuric spots over both legs and two similar lesions over the left arm. The lungs were clear to percussion and auscultation. There was no enlargement of the heart; the point of maximal impulse was felt in the fifth interspace inside the midclavicular line, the heart rate was 80, the rhythm regular, and no murmurs were heard. The liver and spleen could not be felt, but there was tenderness to palpation in the epigastrium and some tenderness in the left upper quadrant.

Laboratory data

On admission the red blood cell count was 4,280,000, the hemoglobin 71 per cent, the white

blood cell count 5,450, with 68 per cent polymorphonuclears and 32 lymphocytes. A specimen of urine was found to have a specific gravity of 1.012, an albumin determination of 3 plus, and was negative for sugar, acetone, bile and urobilinogen; microscopic examination of the urine revealed 40 to 50 red blood cells per high power field and 3 to 6 white blood cells. The icterus index was 34 units. The guiac test was negative. The sedimentation rate was 34 corrected, the hematocrit 32, and prothrombin 100 per cent.

Clinical course

It was first thought that the patient had infectious hepatitis, and she was placed on a high-protein, high-carbohydrate, moderate-fat diet, and on bed rest with bathroom privileges. She was given codeine and Empirin for headache. On the second hospital day nausea and vomiting developed. She was given 1,000 cc. of glucose and saline, and 1,000 cc. of glucose and water. A flat film of the abdomen showed a small calcification in the right pelvis and a similar but less obvious shadow over the left pelvis, which the radiologist felt were phleboliths. Agglutination tests for Weil's disease were done and found to be positive (1:00) for **Leptospira canicola** and **Lept. icterohaemorrhagiae.** A second urinalysis showed 4 plus albuminuria. The cephalin flocculation test was negative at 24 and 48 hours.

The jaundice became worse on the third hospital day, and the patient was started on ACTH, 10 units every six hours. On the fifth day she had improved, not having vomited in 36 hours, and wanted to go home. It was noted, however, that the number of small purpuric spots on her legs and hands had increased.

On the sixth hospital day the patient's hemoglobin suddenly dropped to 37 per cent and the red blood cell count to 2,000,000. She became semicomatose. An osmotic fragility test was entirely normal; a reticulocyte count was 12.4 per cent, and a platelet count was 20,000. The blood urea nitrogen was 38. A direct Coombs test was negative. She was given 500 cc. of O-positive whole blood immediately and an additional 1,000 cc. on the next day. A second platelet count was 22,000. The clotting time was 6 minutes and bleeding time 6 minutes, 30 seconds. The serum alkaline phosphate was 4.8 Bodansky units.

On the seventh day the patient became extremely irrational, began to pick at the bedclothes, and did not recognize members of the family. On the eighth day her respiration became rapid and grunting, and a flaccid paralysis of the left arm and transient paralysis of the right side of the face developed. In view of the above findings the diagnosis of thrombotic thrombocytopenic purpura was made, and she was started on cortisone, 25 mg. every four hours. Additional laboratory studies gave the following results: red blood cells, 2,050,000; hemoglobin, 37 per cent; white blood cells 12,300, with 65 polymorphonuclears, 5 myelocytes, 10 juveniles, and 9 lymphocytes. Van den Bergh's test for serum bilirubin: total, 16.5 mg. per 100 cc. (direct, 3.8 mg.; indirect, 12.7 mg.). The urine was still negative for urobilinogen and bile.

On the tenth hospital day the patient was still delirious, running a temperature of 103 F., rectally, and was entirely unresponsive. She was given 1,000 cc. of whole blood the next day. She began to have convulsive seizures lasting from one to three minutes which were only partially controlled by paraldehyde. The patient continued to have a high fever, began to have more more frequent convulsions, and quietly expired at 4:40 A.M. on the twelfth hospital day.

Pathologic studies

At autopsy the body was that of a moderately well nourished, well developed white female. There was moderate icterus of the skin and sclerae. Petechiae were found over the entire body, and a few ecchymoses were found on the shins.

The heart weighed 325 Gm. There were many petechiae of the epicardium and ecchymoses of the auricular appendages. The liver weighed 1,750 Gm. The surface was smooth except for a slight gray thickening in scattered patches. There were a few petechiae beneath the scalp, and petechiae on the inner aspect of the dura. After the brain was fixed, a notable feature was the presence of petechiae in an irregular distribution.

There was a necrotizing arteriolitis, with numerous fresh and organizing hyaline and granular eosinophilic thrombi in the following organs: skeletal muscle, myocardium, liver, stomach, adrenals, kidneys, pons, and vertebral marrow.

Review of the Literature

Many terms, have been employed to describe this disease, and, although none are entirely satisfactory, S i n g e r ' s [2] designation, "thrombotic thrombocytopenic purpura," is the most common and apparently is accepted at the present time. It does not emphasize, however, the hemolytic anemia as an essential feature of the disease, and Adelson[4] suggests thrombolytic thrombocytopenic purpura as a better descriptive term.

Etiology

Little is known about the causative mechanisms underlying this disease. The original "platelet thromboses" hypothesis, assuming that the occlusions were composed exclusively of p l a t e l e t s, has been discarded[5]. It is now established that the occlusions are not merely due to agglutinated platelets, that the vascular wall is probably affected, and that the anemia is caused by

an extracorpuscular hemolytic mechanism which also damages transfused red cells at a rapid rate[3]. Hyersensitivity mechanisms have been considered but not proved.

Pathology

Histologically, the condition is marked by multiple hyaline thrombi throughout the small arteries, arterioles, and capillaries in most of the organs of the body—most commonly the myocardium, the capsular zone of the adrenals, the renal cortex, the pancreas, and the brain, where they are confined almost exclusively to the gray matter[3]. By various staining techniques it has been shown that the thrombi show the same staining reactions as do the platelets. It is believed but not proved that the thrombotic material is partially made up of agglutinated platelets[6].

Opinions differ as to whether a primary vascular lesion occurs first, followed by an occlusion of the vessel with agglutinated platelets. Most of the evidence, although not conclusive, favors a destructive lesion of the vascular wall of the small blood vessels, followed by dilatation of the vessel, then thrombosis[7]. It is believed that whatever causes the underlying process, it is repetitive, and that the lesions occur in crops[8].

At autopsy petechiae and ecchymoses are seen in various organs. Many pathologists have found lesions of polyarthritis and/or lupus and disseminated platelet thrombosis in patients, and suggested that thrombotic purpura may belong to the collagen group of diseases[9].

Symptoms and Signs

There are two recognized forms of the disease: an acute form, which is fatal within a few days to a few weeks; a chronic form, with relapses, lasting for several months and ending in an acute exacerbation.

In the acute form all the signs and symptoms in any thrombocytopenic purpura, such as petechiae, ecchymoses of the skin, and bleeding from all body orifices, may be seen. Other signs usually present are prolonged bleeding time, positive tourniquet test, and poor clot retraction. Some patients have thrombocytopenia, but only slight or no purpura. Many give a history of upper respiratory infection preceding the illness. Dizziness, nausea, vomiting, headache, malaise, anorexia, and a temperature ranging from 100 to 102 F. are usual complaints. Manifest or latent jaundice of the acholuric, hemolytic type is present. Bilirubinuria is not found. The liver and spleen are moderately enlarged in about half of the patients, microscopic hematuria is almost always found, and nephritis has been encountered. Almost all the patients have some mental symptoms. They may have confusion, irritability, delirium, stupor, or coma. These symptoms are generally transitory and are followed by lucid intervals. Vertigo, facial weakness, hemiplegia, ptosis, and dysphagia are focal signs that may be present[3].

An unusual laboratory finding not found in any other type of spherocytic hemolytic anemia is intermittent spherocytosis. Intermittent increase in osmotic fragility occurs. The Coombs test, which demonstrates the presence of a globulin coat on the surface of red cells, is generally negative; however, in a recent case reported by Ambrosius[10] this test was positive. The leukocyte count is normal or slightly elevated. A leukemoid reaction with immature granulocytes has been observed. Platelet counts are almost always low[3].

Random muscle biopsies are not supposed to be helpful, but in the case presented all specimens taken at random *post mortem* showed typical lesions. The bone marrow shows a nonspecific pattern, but a hyperplastic marrow is generally found present[3]. Cooper[11] found that the best way to demonstrate the lesions by sternal marrow sections was to use paraffin section of marrow.

Only a few cases of chronic intermittent thrombotic purpura have been reported; one patient lived two and one half years and one nine months, both having had splenectomy[3].

Treatment

From the standpoint of treatment, splenectomy has been purely empirical and used only in a few patients because of lack of diagnosis. Splenectomy has been performed in 9 patients: in 7 no effect was noticeable; the other 2 had only temporary remissions. ACTH and cortisone have been used in most instances with poor results. Platelet transfusions are probably of no value, since the platelets are rapidly removed from the circulation in thrombotic purpura. Anticoagulants are valueless and dangerous. Blood transfusions maintain life but usually cannot

elevate the red cell level for any length of time owing to the extracorpuscular hemolytic mechanism[3].

Summary

A case of thrombotic thrombocytopenic purpura and a brief summary of available knowledge on the subject are presented.

The diagnosis of thrombotic thrombocytopenic purpura should be suspected in any patient presenting the triad of thrombocytopenic purpura, hemolytic anemia, and bizarre neurologic signs and symptoms.

Muscle biopsy at random, as demonstrated in this case, may contribute to diagnosis.

The necrotizing arteriolitis so prominent in this case lends support to the theory that small blood vessels are primary affected first by some causative agent in this disease.

Acknowledgement

The author wishes to thank Dr. Leonard J. Rabold, Dr. William G. Murray, and Dr. Joseph B. Stevens for their assistance in preparing this paper.

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Serial esophagoscopic evaluations, with portal pressure determinations in some cases, were made of the esophageal varices of 133 patients with biopsy-proved cirrhosis over an average period of 32.6 weeks. It was found that the varices were notably variable in diameter and extent from time to time, with only the slightest tendency to improve as the general clinical course improved and to worsen as the clinical course worsened. The fluctuations demonstrated some degree of increasing stability as the varices became larger and more extensive. There was no correlation between the apparent duration of the cirrhosis and either varix severity or stability. In a quarter of the patients, at least, one of the examinations showed that the varices had disappeared, but this proved to be temporary disappearance whenever the subsequent course could be adequately followed. In some patients varices disappeared and reappeared very rapidly, these changes being usually without relationship to changes in the general clinical state. The level of the portal venous pressure showed no correlation with the diameter or extent of the varices, and could not be estimated even roughly from the esophagoscopic appearances. The pressure, like varix severity, varied considerably from time to time, without relation to changes in the clinical picture. In the individual patient, however, it was found that varices did not become smaller when the pressure rose or larger when it fell.—Palmer, E. D.: Esophageal Varices Secondary to Portal Cirrhosis, Arch. Int. Med. 47:25 (July) 1957.

Clinical Note: Adult Death from Salicylate Poisoning

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Salicylates, particularly acetyl salicylic acid (aspirin) have been family medicinal landmarks for so long that we have lost fear of the familiar and seldom regard these agents as dangerous. It takes time, however, for children to learn about the contents of medicine cabinets, so that cases of salicylate poisoning in children are relatively frequent[1]. Accidental ingestion, dosage errors, and the large doses employed in treating rheumatic disease may produce intoxication in children; rarely dermal absorption of methyl salicylates and hypersensitivity are means of poisoning. The clinical picture of salicylism in children then should be well recognized. In adults the problem is much less common, although rheumatologists have more than passing acquaintance with the milder manifestations. Occasionally salicylates are used in suicide attempts; because a recent such attempt succeeded, it is thought appropriate to review briefly the clinical picture of salicylate poisoning.

Case Report

The patient, a 33 year old married mother of three young children, took an estimated 30 Gm. of acetyl salicylic acid and undetermined amounts of Bufferin* and meprobamate at about 8:00 A.M. on the day of admission. Shortly thereafter she slashed both wrists. After these lacerations were repaired, she was sent to us for psychiatric evaluation. Except for signs of depression, she was not uncomfortable until about three hours after ingestion, when she vomited profusely five or six times. En route she became stuporous and on arrival was admitted for treatment about eight hours after salicylate ingestion.

Admission blood pressure was 130 systolic, 50 diastolic, pulse rate 120, respiratory rate 44, rectal temperature 106 F. The patient was comatose and considered moribund on admission; her skin was hot and sweaty while her respiratory excursions were rapid and deep. Shortly after admission she had a generalized convulsion and died. Limited laboratory studies included a carbon dioxide combining power of 11 milliequivalents per liter and a serum salicylate level of 117 mg. per 100 cc.

Comment

After ingestion salicylates can be measured in the blood within 30 minutes, peak levels which persist for four to six hours being obtained within two hours. From 50 to 80 per cent of the ingested dose is bound by protein with the unbound fraction, increasing with total dosage. Of the 70 to 80 per cent of a given dose excreted by the kidney, one half is excreted after 24 hours, with traces being present even at 48 hours[2].

At usual doses of 0.3 to 0.6 Gm. every four hours, symptoms are usually minimal if present. At the therapeutic level of 30 to 50 mg. per 100 cc. a variety of manifestations which disappear promptly when the drug is discontinued may occur—headaches, dizziness, tinnitus, deafness, blurred vision, nausea, and vomiting. When a serum salicylate of 50 mg. per 100 cc. is reached, hyperventilation develops and with increasing levels increased agitation, garrulousness, tremor, seizures, coma, and occasionally as in this case death occurs[2].

If poisoning is not severe, treatment is simple: supportive measures and withdrawal of the drug or decrease in dosage if symptoms develop during salicylate therapy. With more serious cases, problems multiply algebraically. One of the early toxic mani-

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*Bufferin-Acetyl salicylic acid with aluminum glycinate and magnesium carbonate.

festations is hyperventilation, which develops because of stimulation of the medullary respiratory centers by the drug and which leads to a respiratory alkalosis[3]. Ordinarily respiratory alkalosis such as seen in hysterical episodes responds to carbon dioxide inhalation, usually rebreathing into a convenient paper bag. In salicylate poisoning the metabolic derangement is much more complex[1c]. The central effect is followed by a peripheral action, with an increase in oxygen consumption, fever, metabolic acidosis, and at times hyperglycemia with glucosuria and ketonuria[2,4]. Urine *p*H does not correlate satisfactorily with the blood *p*H, while carbon dioxide combining power is depressed in both respiratory alkalosis and metabolic acidosis; serum chloride is usually elevated in both conditions. Serial blood *p*H determinations then become a necessity in recognizing the stage of the process and in planning treatment. (Diabetic coma is easily ruled out in most instances because of the marked sweating and because the blood sugar is not increased as greatly in salicylate poisoning.)

When metabolic acidosis supervenes, adequate fluid balance and urine flow must be maintained. Intravenous sodium bicarbonate has been suggested at this stage, as has 1/6 molar sodium lactate. Since these solutions are alkaline, the blood *p*H should be known before administration so that alkalosis, if present, is not exagerated by injudicious use. Because *p*H meters are not standard equipment in most hospitals, dextrose and saline solutions are safer in most cases. Oral sodium bicarbonate has been suggested, but this agent hastens the absorption of salicylate and should not be given before gastric lavage. Since some salicylate may remain in the stomach as late as eight hours after ingestion, the stomach should be lavaged routinely up to this time; normal saline seems preferable.

The use of carbon dioxide inhalation serves no purpose at any time, although oxygen may be effective in combatting hypoxia. Theoretically dialysis with an artificial kidney to remove salicylates[5], exchange transfusions, and hypothermia are attractive; logistical problems make dialysis a conversation piece in most hospitals, while availability of blood usually limits exchange transfusions to children. Hypothermia by depressing the accelerated body metabolism could conceivably allow more time for excretion of the offending agent, although no helpful data are available.

Not to belabor the obvious, but prevention is the best treatment. All drugs should be kept away from children and all dosages carefully checked by parent, patient, and physician. With adults intent on suicide, physicians should be aware that salicylates may be neither respectful nor friendly.

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The Medical Spectator

THE GREAT CHOLESTEROL CRISIS

Seen in historical perspective, the present cholesterol crisis takes on cultural aspects hardly glimpsed if one neglects such real and fictional characters as Ponce de Leon, Brown-Sequard, Dr. Brinkley, Faust, and Mr. Am. This quintet dramatizes man's struggle with aging and with ignorance, each member seeking or possessing the secret of life. For one the hope was geographical; another offered "glands" surgically, while the third suggested "glands" by mouth. Faust contracted with the Devil and Mr. Am with the Chicago Tribune-New York Daily News Syndicate. The least common denominator, or rather the most common trait displayed, has been wishful thinking.

Separating hope and fact has ever demanded rigorous thought, careful experiment, and reluctance to inhabit a world solely black and white. How economic factors, fashion, anxiety, and fear influence the epidemiology of drug consumption was touched on in the last issue. The great cholesterol crisis (hereinafter referred to

as GCC) offers an unparalled opportunity to explore the bull market in medicines.

Certain elements of the GCC can be noted:

1. Hardening of the arteries is a manifestation of aging.

2. Most people do not think aging is a good thing even though other cultures have respected the aged and looked to the elderly for wisdom and sound advice.

3. Hardening of the arteries is characterized by intimal lipid changes.

4. Blood cholesterol measures a lipid.

5. There is a poorly defined relationship between hypercholesterolemia and atherosclerosis.

A ready conclusion after superficial study would be: lower the cholesterol and decrease the atherosclerosis. Many agents have been shown to decrease blood cholesterol; a partial list would include estrogens, thyroid substance, lecithin, sitosterol, niacin, alpha tocopherol, cornoil, safflower seed oil, cortisone, and corticotropin. Yet what changes in the internal environment are induced by lowering the cholesterol are even less understood than the role of cholesterol in the pathogenesis of atherosclerosis. An advertisement describing the virtues of a particular emulsion of unsaturated fatty acid and mixed tocopherols in lowering the blood cholesterol is not in itself fallacious; by leaving the unsaid unsaid the advertiser strongly intimates that this lowering is good and true.

This may well be good and true, but implying it doesn't make it so. The reason for this is our own ignorance of the pathogenesis of atherosclerosis. Nothing is said in the blurb referred to above of heredity, vessel wall anatomy, blood pressure, dietary fat and calories, sex, and that glorious catch-all factor — stress. We have again been reminded that fat and cholesterol are not synonymous and that the arterial wall can synthesize cholesterol from various substances[1].

We do not yet know when an atheromatous lesion is irreversible, nor are we sure how essential essential fatty acids are. Recent evidence does suggest strongly that saturated fatty acids favor an acceleration of the atherosclerotic process. Clinical studies of populations who ingest greater quantities of unsaturated fatty acids of vegetable or marine origin and less saturated fatty acids (animal origin) do indicate less disease in the former groups[2]*.

We still do not know what determines the site of an atheromatous plaque. Our understanding of the genetic factors at work is fuzzy at best, while our methods of defining the extent of the disease and its prognostic importance in human beings are woeful.

It cannot truthfully be said that a lowering of the serum cholesterol indicates arrest of the process, nor have we evidence that any hypocholesterolemic agent mobilizes intimal lipids and thereby improves arterial wall function in a manner analogous to the urate mobilizing effect of probenecid.

Certain conclusions do seem justified:

1. Cholesterol is somehow involved in the atherosclerotic process.

2. Blood cholesterol can be lowered.

3. Carefully controlled studies of morbidity and mortality over a long period of the use of hypocholesterolemic agents are necessary before any promise can be made to the general public.

These conclusions certainly do not justify the hoopla now being dispensed to induce the GCC. These conclusions do not contraindicate switching to skimmed milk; after all, a quart of skimmed milk is 8 to 10 cents cheaper than a quart of whole milk, besides containing less fat.

*Unsaturated fatty acids contain one or more carbon-carbon double bonds, while saturated fatty acids contain none, thereby being saturated in this respect.

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THIRD PARTY ENCROACHMENT

President Schoenheit's Message this month is so important that it is featured on the cover of this issue. In recognition of the increasing number of non-medical agencies involved in the private practice of medicine, the House of Delegates, at the last meeting of the State Society, voted to sponsor a Survey of Third Party Encroachment on the Private Practice of Medicine. Mr. Horace Cotton, who is well qualified by his long association with doctors, has been selected to direct the survey. In order for it to succeed, however, the surveyors will need the whole-hearted cooperation of the State Society members.

As stated in the President's Message, every member of the society will receive a form to be completed, giving his experience with third parties, and his opinion, pro or con, about such encroachment. If the survey is to mean what it should, it is highly important that far more than the average proportion of these forms be returned. It is hoped that every member who reads this will do at least two things: (1) fill out his own form promptly; and (2) talk to as many of his colleagues as possible and remind them to do likewise.

* * *

POSTGRADUATE MEDICINE IN NORTH CAROLINA

Within the memory of our older members, the time was when a North Carolina doctor who felt the need of what Osler called a "brain dusting" had to go out of the state for postgraduate instruction. This was not only expensive, but the doctor had to leave his practice for the duration of the course. To meet this need of postgraduate training, the University of North Carolina 40 years ago sponsored a series of postgraduate courses that were the first of their kind in the nation. A visiting lecturer, in the fashion of a Methodist circuit rider, covered his territory every week, giving lectures to a different group of doctors, in a different town, every day. This plan enabled the doctors to get the equivalent of a week's intensive postgraduate training by giving up an afternoon a week. The idea has since been copied by a number of other states.

This program, in a modified form, is still in operation. Its forty-first year offers a six-week course in the First District on Wednesdays, beginning January 15, rotating between Ahoskie, Edenton, and Elizabeth City. One day later—January 16—a similar course, sponsored by the Wake County Medical Society in cooperation with the University of North Carolina School of Medicine, begins in Raleigh. The meetings will be held every Thursday.

In addition, the University of North Carolina is offering a symposium on November 21-22, at North Carolina Memorial Hospital. On February 7 the State Medical Society and the University of North Carolina Medical School will sponsor an Occupational Health Seminar.

Duke University offers every Thursday, at 10 A.M., a lecture by one of the services, followed by a clinicopathologic conference and medical staff rounds. The school will

offer also a postgraduate course in gastroenterology on February 10-14 and a course in rheumatology on March 10-11.

The Bowman Gray School of Medicine of Wake Forest College offers weekly on Monday nights at 7:30 P.M., a scientific speaker or clinicopathologic conference. It will also offer a postgraduate course in gastroenterology in March and another in obstetrics, gynecology, and pediatrics in April (specific dates to be announced later). The latter will be sponsored in cooperation with the Personal Health Division of the North Carolina State Board of Health.

While it is stimulating and instructive to attend one or two national or large regional meetings a year, it is no longer necessary to leave the state in order to keep up with medical advances.

* * *

STATE JOURNAL CONFERENCE

For many years it was customary for the editors of state medical journals and secretaries of the state medical societies to be guests of the American Medical Association tion at its headquarters in Chicago. A few years ago the State Medical Journal Advertising Bureau was reorganized as an autonomous organization, with offices outside the A.M.A. headquarters building. The value of the meeting of minds in the conferences was so great that it was decided to continue them under the sponsorship of the S.M.J.A.B., but to hold them only every two years, instead of annually, and to include business managers and associate editors, instead of state society secretaries. The conferences are still held in the auditorium of the A.M.A. headquarters, and the A.M.A. serves lunches on both days of the conference.

The third of these biennial conferences was held on Monday and Tuesday, October 28 and 29. The NORTH CAROLINA MEDICAL JOURNAL was represented by the editor and the business manager.

While the conference was devoted largely to the technical side of medical journalism, a summary of its high lights may be of interest to some of our readers. The chairman, Dr. Everett George, editor of the *Journal of the Iowa State Medical Society*, had arranged a program that was profitable to all present.

Since Secretary George Lull was away, Dr. Julian Price, representing the Board of Trustees, took his place and gave the address of welcome. His was a very fitting selection, since he was for many years editor of the *South Carolina Medical Journal* and a former member of the Advisory Committee of the State Journal Advertising Bureau. His address, though brief, was marked by his characteristic combination of humor and philosophy.

Monday afternoon was devoted to two workshops: one, conducted by Mr. O. M. Forkert, on journal format and make-up; the other, conducted by Mr. Jackson, on advertising problems.

At the dinner Monday evening, at the Sheraton Hotel, the group relaxed and enjoyed a humorous address by Mr. Carl F. Conway, a lawyer of Osage, Ohio.

Tuesday morning was devoted to a panel discussion of the various problems of medical journals. Members of the panel were Dr. Joseph Garland, editor of the New England Journal of Medicine; Mr. Alex H. Stewart, managing editor of the Pennsylvania Medical Journal; and Mr. Alfred Jackson. Dr. Stanley Weld, editor of the *Connecticut Medical Journal*, discussed the problems of the Advertising Committee of the Bureau. Dr. Lee Hill, of Des Moines, Iowa, told of the problems of the specialty journals, in contrast with the state journals. Tuesday afternoon was given over to Mr. Forkert for questions and answers.

Without disparaging any of the others on the program, Mr. C. M. Forkert was the star of the show. He knew every detail of the printing business and held the audience literally spellbound for two hours on Monday afternoon. On Tuesday morning he held an unscheduled round table discussion with those fortunate enough to arrive early, in which he offered numerous constructive criticisms of individual journals. During the lunch hour he resumed this discussion, and through the regular sessions he was ready with pertinent suggestions.

Mr. Forkert seemed never to tire; was never out of patience; and his keen sense of humor softened his criticisms, all which were taken with good grace by the individual editors. He said that there had been great improvement in all the state journals since the last conference two years ago, and that they had "made as much progress in a short time as any group I've ever known."

President's Message

THIRD PARTY ENCROACHMENT

There Can Be Only One Topic

. . . for my message this month. It is the topic which, I earnestly hope, is presently in the minds of all our members and under discussion wherever two or more North Carolina physicians are gathered together. It is the topic of Third Party Encroachment on the Private Practice of Medicine in our State. And let us realize that the subject is not occupying our thoughts alone. All over the United States doctors are realizing that the problem of the multitudinous agencies, organizations, firms, and individuals who interpose themselves between the physician and his patient is a problem to the solution of which the profession holds the key.

"Ripeness is all," said the Bard. Ripeness —ripeness for clearsighted, factual study— is what this problem has. Recognizing this fact, we in North Carolina have voted to make this study before overripeness sets in, for we know that if we sit on our hands, waiting for the other fellow to do it, the fruit that finally falls will be bitter. The House of Delegates took a bold and imaginative decision when it voted to sponsor a Survey of Third Party Encroachment. We whom you have chosen as your Executive Council are ready to be bold and imaginative in framing recommendations for action based on the Survey's findings. But first we must have the findings. The basic material for them can come only from you. In the words of one of the great war leaders, "Give us the tools and we will finish the job."

Read again the definition of Third Party Encroachment sent to you by our surveyors: "Where any agency, organization, company or person intervenes between a private practitioner (*i.e.*, one rendering service for fees in his own right) and a patient, in such a manner as to deny the patient free choice of doctor, or the doctor free choice of patient, or to direct the doctor as to the management of the case, or to limit or influence the nature or extent of the doctor's professional services *by way of fee or otherwise*, there is encroachment."

Do we not all see that encroachment is everywhere? It steals up as silently as the dawn. It is for us to see that it does not bathe us in the illusory radiance of a false dawn, followed by a blacker night than before. As Westbrook Murphy told us at Pinehurst last year, these third parties "have no souls, have no consciences, cannot exercise professional judgment, and are impersonally ruthless." No power of divination, no gift of second sight, no special prescience is required to see what is staring us in our professional face: Some day the third parties are going to form a Third Party, a combination to control medicine itself, to demote it from art to craft, and to downgrade us who profess it to those who supply it . . . gift-wrapped as directed.

I do not know, any more than you do, what the Survey findings will be. Nor do I know what recommendations your Executive Council will make (even *can* make) after it has studied whatever facts the Survey may turn up. There is no demand upon me to prophesy these things. But there is a demand upon me to insure, so far as I am able, that the seed we have sown shall germinate, that the Survey shall not perish from the inertia of those for whose benefit it was conceived.

Each member of the Medical Society of the State of North Carolina has or will soon receive a form to be completed in our efforts to compile the facts of Third Party Encroachment in North Carolina. Please do not disregard it: use it!

If, as an individual, you have experienced detrimental third party intervention, mail the facts to our surveyors. If, as an individual, you have a point of view to express (in defense of third parties, if you like), go ahead and use the report form for that purpose. If your local society has not yet had it discussion of third party encroachment, do what you can to push it along so that the collective voice of your medical community shall not go unheard. As President, as physician, as fellow man, I ask you to give your knowledge and wisdom in this truly worthwhile project.

E. W. SCHOENHEIT, M.D.
with
HORACE COTTON,
Director of Survey

CORRESPONDENCE

North Carolina Cancer Institute

To the Editor:

I am writing to you in regard to certain information concerning the North Carolina Cancer Institute at Lumberton. At a meeting on September 15, of the Executive Committee of the Board of Trustees, they requested that I write to you concerning admission policies.

The institute is now licensed as a chronic disease hospital as you probably know. The major change is that in certain instances, where it is deemed advisable, various chemotherapeutic and hormone drugs may be administered to the patient with the hope of ameliorating the patient's condition. The important items we would like brought to the attention of the physicians are:

Item I: Only patients who are certified as indigent or medically indigent by their Welfare Department will be accepted in accordance with the wishes of the cancer committee of the State Medical Society.

Item II: Only patients who have proven cancer and who have already had the usual standard surgical and radiological therapies as indicated or who have been definitely judged to be beyond the stage where such treatment would be of benefit can be admitted.

Item III: There must be a request from the patient's attending physician for admission of the patient. This statement must certify that the patient has cancer proven by biopsy except in rare instances where the overwhelming evidence is in favor of cancer and the proof of such would require a major operation which would be detrimental to the patient's immediate life.

The North Carolina Cancer Institute wishes to be of service to those patients who are in need of its care, but does not wish to admit any patient whose attending physician does not feel that the patient rightfully belongs there.

Sincerely yours,

H. Max Schiebel, M.D., President
The Board of Trustees
North Carolina Cancer Institute

BULLETIN BOARD

COMING MEETINGS

North Carolina Board of Medical Examiners, meeting to interview candidates for licensure by endorsement—Mid Pines Hotel, Southern Pines, January 11.

University of North Carolina School of Medicine weekly postgraduate programs: First District Medical Society, alternating between Ahoskie, Edenton, and Elizabeth City, beginning January 15 and continuing Wednesday afternoons and evenings through February 22; Raleigh, beginning January 16 and continuing Thursday afternoons and evenings through February 23.

Duke University Postgraduate Course in Gastroenterology—Durham, February 10-14.

Watts Hospital Symposium—Durham, February 12-13.

A.M.A. Eleventh Annual Clinical Meetings—Convention Hall, Philadelphia, December 3-6.

American College of Surgeons, Sectional Meetings, Jackson, Mississippi, January 16-18.

A.M.A. Industrial Health Congress—Milwaukee, Wisconsin, January 27-29.

Fifty-Fourth Annual Congress on Medical Education and Licensure—The Palmer House, Chicago, February 9-11.

New Members of the Society

The following new members joined the Medical Society of the State of North Carolina during the month of October, 1957:

Dr. Robert Paul Davis, UNC School of Medicine; Chapel Hill; Dr. Richard Lawrence Dobson, N. C. Memorial Hospital, Chapel Hill; Dr. Allan Watson Downie, N. C. Memorial Hospital, Chapel Hill; Dr. John Carroll Herion, Circle Drive, Dogwood Acres, Chapel Hill; Dr. Martin Harvey Keeler, N. C. Memorial Hospital, Chapel Hill; Dr. Cornelius Lansing, 309 Briarbridge Valley, Chapel Hill; Dr. Eugene Wiliam Loeser, Jr., 18 Audley Lane, Chapel Hill; Dr. Walter Coles Lusk, II, Box 3317, Duke Hospital, Durham; Dr. Richard Lee Murtland, UNC School of Medicine, Chapel Hill; Dr. Arthur Jergen Prange, Jr., Rt. 2, Sherwood Forest, Chapel Hill; Dr. Albert Jack Silverman, Duke Hospital, Durham.

Dr. John Lewis Simmons, UNC School of Medicine, Chapel Hill; Dr .William Jeoffrey Wysor, Jr., N. C. Memorial Hospital, Chapel Hill; Dr. Daniel Test Young, 410 McCauley Street, Chapel Hill; Dr. William Glenn Young, Box 3617, Duke Hospital, Durham; Dr. Charles Granger Chapman, Mercy Hospital, Charlotte 5; Dr. Griffin Caswell Daughtridge, 526 Marigold Street, Rocky Mount; Dr. Irvin George Scherer, Union Grove; Dr. Gordon Cameron Crowell, 709 South Aspen Street, Lincolnton; Dr. James Francis Morris, 306 North

Taylor Street, Goldsboro; Dr. Talbot Fort Parker, Jr., 401 North Herman Street, Goldsboro; Dr. James Manning Walker, 15 East Jordan, Brevard.

Dr. Robert Donald Higgins, 1204 Cowper Drive, Raleigh; Dr. Jean Douglas McRee, Box 7573, State Hospital, Raleigh; Dr. John White Gainey, Jr., 105 North 10th Street, Morehead City; Dr. James Foster Crosby, 916 Bridle Path Lane, Charlotte; Dr. Alfred Schick, Mercy Hospital, Charlotte; Dr. Hervy Basil Kornegay, Jr., 323½ Grove Park Avenue, Winston-Salem; Dr. Paul Osman Howard, 550 Summitt Drive, Sanford; Dr. Alfred R. Cordell, Bowman Gray School of Medicine, Winston-Salem; Dr. Charles G. Gunn, Hanes Hosiery Mills, Winston-Salem; Dr. Charles C. Stamey, 720 West 5th Street, Winston-Salem; Dr. William C. Sugg, 625 Reynolds Building, Winston-Salem; Dr. Robert Key Arthur, Jr., 519½ North Main Street, High Point.

News Notes from the Duke University School of Medicine

Dr. E. C. Hamblen, Duke gynecologist and endocrinologist, has been invited to visit six countries during a three-month lecture and teaching tour. He will lecture and conduct postgraduate courses at the invitation of various Latin American universities and professional societies.

Highlight of the tour will be his appearance as a featured speaker for the seventh national meeting of the Chilean Society of Obstetrics and Gynecology, December 1-4 in Santiago, Chile. Also, he will conduct a three-week postgraduate course in gynecologic endocrinology at the University of Chile.

A Duke medical faculty member since 1931, Dr. Hamblen is a specialist in the field of reproductive endocrinology. He has written four books that include "Facts for Childless Couples" and "Facts About the Change of Life."

* * *

Weekly Tumor Conferences bringing together the various groups which manage neoplastic disease are being held each Wednesday at 11:30 a.m. in the new Surgical Private Diagnostic Clinic at Duke Hospital.

Discussions center in the management of individual patient problems, but reports on research and general experience are also planned.

* * *

Duke University has received two U. S. Public Health Service grants totaling some $84,000 to expand and improve research laboratory facilities at the University's Medical Center.

One grant of $42,000 will be used to expand the Center's tissue culture laboratory for study of tumor-producing viruses. The other grant, also worth $42,000, will provide for the equipping of a new laboratory for physiological studies of pathogenic (disease causing) fungi.

Dr. Joseph W. Beard, professor of surgery and associate professor of virology, is the principal investigator for tumor virus studies now under way at Duke. This work includes culture of leukemia cells and virus-induced tumors and study of factors that influence virus production by cells.

Dr. Leo Pine, assistant professor of microbiology, will be principal investigator for research in pathogenic fungi. Among areas of investigation will be the metabolic processes of pathogenic fungi and factors influencing their growth and ability to cause disease.

* * *

Leonard C. Small has been appointed administrative assistant at Duke Hospital, Superintendent F. Ross Porter announced recently.

He succeeds John M. McBryde, Jr., who resigned to accept a position as assistant superintendent of Good Samaritan Hospital in Lexington, Kentucky.

* * *

"Brain chilling" research that may open the way to new chemical treatment of cerebral tumors and also permit surgeons to conduct brain operations now considered impossible is under way here at the Duke University Medical Center.

Duke neurosurgeon Barnes Woodhall is director of the project, which centers around cooling the brain to a temperature at which virtually all brain activity ceases.

Dr. Woodhall and his associates have successfully lowered the brain temperature of dogs from a normal 100 to 50 F. They hope within a year to begin applying the process to human beings.

Key to the possibilities opened by this cooling process, known as cerebral hypothermia, is the fact that at such low temperature the brain's need for blood and oxygen ceases.

This means that surgeons may operate on a virtually bloodless brain to correct conditions such as faulty brain arteries—now considered inoperable.

Another goal of the Duke research is a new type of chemical treatment for brain tumors. This process would involve cooling the brain, withdrawing its blood supply, and pumping in a chemical solution to stop or slow the growth of tumor cells. After a period of several hours, the blood supply would be restored and the brain temperature brought back to normal.

Members of the Duke research team in addition to Dr. Woodhall are Dr. David H. Reynolds, Dr. Annabelle Craddock, Dr. Yao Chang Chien, Miss Barbara Matthews, and Stephen Mahaley. Dr. Woodhall recently reported on the project at the First International Congress of Neurological Surgery held in Brussells, Belgium.

The hypothermia experiments are being conducted under provisions of a $30,388 research grant from the National Institute of Neurological Diseases and Blindness, U. S. Public Health Service.

News Notes from the University of North Carolina School of Medicine

Physicians from the two Carolinas and Virginia have been invited to a symposium to be held at North Carolina Memorial Hospital on November 21 and 22.

Registration will begin at 8:30 a.m. in the lobby of the hospital. At 9:30 a workshop in cardiology begins with small group discussions of individual cases. Participants are invited to bring their own stethoscopes. Synopses of the cases to be discussed will be sent to advance registrants. Thursday afternoon's program will offer a panel discussion of selected cardiac cases by members of the School of Medicine faculty and Dr. Truman G. Schnabel, associate professor of medicine, University of Pennsylvania School of Medicine.

The program for Friday will begin at 9:15 a.m. with a discussion of Urological Problems in the Female by Dr. Houston S. Everett, associate professor of gynecology at the Johns Hopkins School of Medicine. Also on Friday members of the School of Medicine faculty will discuss Heart Disease in Pregnancy, Problems of Perinatal Mortality, Diagnostic Evaluation in Viral Diseases, Radiation Health, Epiphyseal Fractures, and Neck Injuries.

Physicians attending the program are invited to bring their wives. A coffee hour will be held for the wives on Friday morning at the School of Medicine. On Thursday evening a social hour and dinner will be given for attending physicians and their wives.

The North Carolina State Board of Health is giving financial assistance to the workshop in Cardiology on November 21.

The symposium has been approved for 12 hours credit by the American Academy of General Practice.

* * *

Dr. Robert A. Ross, professor and head of the Department of Obstetrics and Gynecology, has been appointed representative of the commandant of the Sixth Naval District.

The announcement of the appointment was made by Capt. S. E. Hughes, Jr., Naval Medical Corps, of the Sixth Naval District Headquarters in Charleston, S. C. The Sixth Naval District is composed of North and South Carolina, Georgia, Florida, Alabama, Mississippi, and Tennessee.

Dr. Ross will aid and advise in the processing of medical students and physicians interested in the Naval Reserve Corps program. He is a captain in the U. S. Naval Reserve and is a veteran of both World War I and World War II. During World War II he saw action in the Philippine, Iwo Jima, and Okinawa campaigns and took part in the occupation of Japan. He was awarded the Purple Heart Medal.

Dr. Ross was active in the organization of the Naval and Marine Corps Training Center in Durham.

* * *

The Department of Bacteriology recently acquired a new professor of biophysics and one of the most powerful electron microscopes in the world. David Gordon Sharp, Ph.D., the new faculty member, is one of the pioneers in the field of electron microscopy, itself a relatively new science. He graduated from Rutgers University in 1932 in physics. In 1936 he went to Duke University as a consultant engineer and to do graduate work. He became Duke's first graduate student in biophysics, and his Ph.D. in physics was granted in 1939. Until he joined the faculty at U.N.C. he worked at Duke, where his major interest was the application of physical methods to the study of virus particles. Dr. Sharp is now also building an ultracentrifuge which will be capable of 50,000 revolutions per minute.

The electron microscope, one of 56 in existence, cost approximately $30,000.

* * *

Dr. Lucie Jessner and Dr. D. Wilfred Abse, both of the Department of Psychiatry, have recently returned from a series of psychiatry meetings in Europe.

They first attended the International Psychonalytic Conference in Paris. From there they went to the Travistock Clinic in London, and then to meetings at the University of Bern in Switzerland.

While in Switzerland Dr. Jessner presented a paper on "Psychosomatic Aspects of Asthma in Children."

The two professors also attended the International Psychiatric Conference in Zurich, Switzerland, where Dr. Abse presented a paper on "Special Problems in Psychotherapy with Schizophrenia." Co-author of this paper was Dr. J. A. Ewing, also of the Department of Psychiatry.

* * *

Plans have been completed for two postgraduate medical programs to be held in Raleigh and the First District in January and February. The First District program will alternate between Ahoskie, Edenton and Elizabeth City, and is co-sponsored by the First District Medical Society. Dr. Archie Y. Eagles of Ahoskie is chairman of the First District Postgraduate Committee. The Raleigh program is co-sponsored by the Wake County Medical Society. Dr. William Senter is chairman of the Wake County Postgraduate Committee.

The First District program will be held for six weeks on Wednesday afternoons and evenings, beginning on January 15. The Raleigh program will meet on Thursday afternoons and evenings for six weeks, beginning on January 16. No meetings will be held on February 12 and 13 because of the Watts Symposium.

A complete program for the courses will be released at a later date. This is the forty-first year since the School of Medicine began sponsoring postgraduate programs for practicing physicians.

* * *

Dr. Robert R. Cadmus, director of N. C. Memorial Hospital of the University of North Carolina, and George M. Norwood, Jr., of the business office of the U.N.C. Division of Health Affairs, were guest speakers at a Columbia, South Carolina, meeting recently.

The two-day institute, which was sponsored by the South Carolina Hospital Association, dealt with financial management and cost findings. Dr. Cadmus spoke on "Administrator's Responsibilities." Norwood spoke on "Accountant's Responsibilities."

* * *

Two faculty members of the University of North Carolina School of Medicine spoke before the meeting of the North Carolina Academy of General Practice held in Asheville on October 14-16.

Also held on October 16 was the Ninth Symposium of the Tenth District Medical Society.

Dr. David A. Davis, professor of surgery in charge of anesthesiology, delivered a paper entitled, "The Effects of Anesthetic Agents on Circulation."

Dr. James Newsome of the Department of Surgery gave a talk entitled "Chemotherapy of Malignancy."

* * *

A $15,000 grant from the U. S. Public Health Service has been made to Dr. Abraham Widra of the University of North Carolina School of Medicine for a three-year research project. The study will deal with the cell structure and genetics of certain pathogenic yeasts. The effects of various drugs on these microorganisms will also be studied.

Dr. Widra was appointed a faculty member in the Department of Bacteriology and Immunology of the U.N.C. School of Medicine in 1955.

* * *

A man and wife team of physicians has joined the facutly of the University of North Carolina school of Medicine. They are Dr. John H. Arnold and Dr. Mary B. Arnold. Both have been appointed instructors in the Department of Pediatrics of the School of Medicine.

Dr. John Arnold is a native of Port Arthur, Texas, and received his undergraduate and medical education at Tulane University. Prior to joining the U.N.C. faculty, he was an instructor at the Tulane Medical School and for the past two years has been a research fellow in pediatrics at the Children's Medical Center, Boston.

Dr. Mary Arnold is a native of Fitchburg, Massachusetts. She did her undergraduate work at Vassar College and received her M.D. from the University of Vermont. Prior to accepting her present position, she was a research fellow in pediatrics at the Massachusetts General Hospital, Boston.

Both physicians are diplomates of the American Board of Pediatrics.

* * *

The University of North Carolina School of Medicine and North Carolina Memorial Hospital staged a scientific and educational exhibit at the State Fair held in Raleigh October 15-19. Featured in the exhibit was an artificial heart machine.

The purpose of the exhibit was to show what has been done by the Medical School and Hospital in connection with the Good Health Program of North Carolina.

One interesting point in the exhibit was the fact that last year the U.N.C. School of Medicine provided instructions to more than five times the number of students enrolled in the Medical School.

This situation is explained by the fact that the School of Medicine gives instructions to students in the U.N.C. Schools of Dentistry, Pharmacy and Nursing, and to students who are seeking degrees in scientific fields outside of the field of medicine.

* * *

Dr. K. M. Brinkhous, professor and head of the Department of Pathology, has returned from Europe, where he attended the International Congress on Clinical Chemistry in Stockholm, Sweden.

While in Sweden he also attended the meeting of the International Committee on Coagulation Nomenclature. He was plenary session speaker at the biennial Congress of the European Hematologic Society in Copenhagen while visiting in Denmark.

News Notes from the Bowman Gray School of Medicine

On November 11, Dr. Paul R. Hawley, retired major general, delivered the third annual Herbert M. Vann Memorial Lecture. Dr. Hawley, the director of the American College of Surgeons, spoke on the subject "Philosophical Aspects of Medicine." Dr. Herbert M. Vann, in whose memory the lectureship was established by the Chi Theta Chapter of the Phi Rho Sigma medical fraternity, was professor of anatomy in the Bowman Gray School of Medicine until his death in 1951.

* * *

The December schedule of programs sponsored by the Bowman Gray Medical Society has been announced:

December 2—Dr. George J. Thomas, chairman, section of anesthesiology, University of Pittsburgh, School of Medicine. Demonstration of anesthetic explosions.

December 16—Dr. E. Cuyler Hammond, professor of biometry, Yale University. "Smoking and death rates—A riddle in cause and effect."

The latter will be sponsored in cooperation with the Sigma Xi Club. Both will be held in the clinical amphitheater at 7:30 p.m.

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At the annual meeting of the North Carolina Ortheopedic Association in Raleigh, Dr. H. F. Forsyth, associate professor of orthopedics, was elected chairman of the newly formed Orthopedic and Traumatic Surgery Committee of the State Medical Society.

* * *

Dr. Courtland H. Davis, assistant professor of neurosurgery, has been elected to the Board of Directors of the National Association for Retarded Children.

* * *

Dr. Camillo Artom, professor of biochemistry, recently presented a paper, "Role of Choline in the Hepatic Oxidation of Fat" before the symposium on "The Mode of Action of Lipotropic Factors in Nutrition" held at the Graduate School of Public Health at the University of Pittsburgh.

* * *

Dr. Warren Andrew, professor and director of the Department of Anatomy, and Dr. Norman M. Sulkin, professor of anatomy, recently presented papers before the tenth annual meeting of the Gerontology Society in Cleveland. Dr. Andrew's paper was entitled "The Reality of Age Changes in the Nervous System," and Dr. Sulkin's was "The Duration of Pigmentation in the Nerve Cell Following Prolonged Administration of Acetanilid."

* * *

Dr. Harold D. Green, professor and director of the Department of Physiology and Pharmacology, recently presented a paper before the New Jersey Diabetes Association. His title was "Medical Management of Occlusive Arterial Diseases in the Diabetic."

* * *

Dr. I. Meschan, professor and director of the Department of Radiology, presented a paper, "Cobalt 60 in the Treatment of Cancer" before the North Carolina Nurses Association, which met in Asheville. He also spoke before the Buncombe County Medical Society on "Roentgen Pathology of the Lung Parenchyma."

North Carolina State Board of Medical Examiners

The Board of Medical Examiners of the State of North Carolina will meet at the Mid Pines Hotel, Southern Pines, North Carolina, Saturday, January 11, 1958, at which time applications for license by endorsement will be interviewed.

North Carolina Society for Crippled Children and Adults, Inc.

Felix S. Barker, Director of the Division of Special Education, State Department of Public Instruction, was elected president of the North Carolina Society for Crippled Children and Adults at the 1957 annual convention held in Durham October 25-26. Mr. Barker succeeds Dr. Leslie B. Hohman of the Duke University School of Medicine.

Dr. Edgar T. Thompson of Durham and J. Preston Wrenn of Charlotte were named vice presidents; Mrs. R. L. Sanborn of Bessemer City, secretary; and W. E. Thompson of Chapel Hill, treasurer. Twelve new directors were also named.

The annual sessions included a number of distinguished speakers. Dr. William deGravelles, director of rehabilitation services at the Duke Medical Center, moderated the opening panel on the rehabilitation of hemiplegics. A panel on the home physical therapy service programs supported by the North Carolina Society for Crippled Children was moderated by Mrs. Eleanore Malone.

Other panels included a discussion on the care of the handicapped aged, moderated by Dr. William P. Richardson of the North Carolina Memorial Hospital, and a discussion of service program for crippled children with Dr. John W. Baluss as moderator.

At the closing banquet Dr. Warner L. Wells spoke on "The Effects of Atomic Fall-out on a Civilian Population."

North Carolina Heart Association

If man had never gotten up off all fours and learned to walk on his hind legs, he might not now suffer from varicose veins, according to Dr. John B. Hickam of Duke, president of the North Carolina Heart Association. Dr. Hickam made the statement in announcing the publication of a new booklet by the American Heart Association entitled "Varicose Veins."

The booklet emphasizes that doctors can help patients ward off serious damage if the condition is caught in time. Many measures are now available to minimize the bulging of the leg veins into unsightly swellings and such complications as swelling around the ankles, irritation of the skin, leg ulcers or sores can almost always be prevented by proper care and treatment.

The booklet is designed primarily for patients with varicose veins and their families, and for physicians to give such patients under their care. Single copies are available free on request to local Heart Associations, or by writing to the North Carolina Heart Association, Miller Hall, Chapel Hill, North Carolina.

Edgecombe-Nash Medical Society

The monthly meeting of the Nash-Edgecombe Medical Society was held on October 9 in Rocky Mount.

This meeting brought together the Nash-Edgecombe Bar Association and the medical society in a joint meeting. The yearly meeting with the legal association serves to foster relations between the two groups and an understanding of medico-legal affairs.

Robeson County Medical Society

The Robeson County Medical Society met in Lumberton, North Carolina, on October 7, at the Lorraine Hotel. Dr. Robert Dobson, Instructor in Medicine, U.N.C., spoke on "Dermatologic Problems in General Practice." Dr. Bob Andrews, pathologist at the Robeson County Memorial Hospital, Lumberton, was introduced as a new member.

News Notes

Dr. Andrew D. Taylor of Charlotte has announced the association of Dr. William P. Coleman in the practice of allergy.

Southern Regional Education Board

Governor Luther H. Hodges of North Carolina was elected Chairman of the Southern Regional Education Board at its annual meeting in Atlanta on September 21.

Also elected at the meeting were Dr. Philip G. Davidson, president of the University of Louisville, vice chairman, and State Rep. Chappelle Matthews of Georgia, secretary-treasurer.

SREB is an agency of the Southern states whose purpose is to help states in sharing their resources for higher education with each other. SREB is supported through legislative funds appropriated by the states.

News Notes from the American Medical Association

A.M.A. Clinical Meeting Planned

Approximately 4,000 American doctors are expected to attend the American Medical Association's eleventh clinical meeting December 3-6 in Philadelphia.

The postgraduate education meeting is aimed at helping to solve the daily practice problems of the family physician, according to Dr. Thomas G. Hull, secretary of the A.M.A.'s Council on Scientific Assembly.

Meetings will be held in Convention Hall and at the Bellevue-Stratford Hotel, where the House of Delegates, the A.M.A.'s policy-making body, will hold sessions.

A.M.A. Plans Industrial Health Congress

Maintaining high standards of health in industry will be a principal topic of consideration at the eighteenth annual Congress on Industrial Health to be held January 27-29 at the Schroeder Hotel in Milwaukee. Physicians, nurses, industrial hygienists, engineers, and others interested in the field will attend the meeting sponsored by the A.M.A.'s Council on Industrial Health.

Recent developments in industrial health programs and various aspects of immunization programs in industry will be among the subjects covered by panelists at a special session co-sponsored by chairmen of state medical society committees on industrial health. Other features include three technical sessions on—(1) general aspects of disability evaluation; (2) industrial dermatitis, causes and evaluation of disability; (3) low back pain, cause, treatment, evaluation of disability, rehabilitation.

A.M.A. Plans New Exhibits in 1958

To reach more and more Americans with authentic up-to-date health information, the A.M.A.'s Bureau of Exhibits announces a number of major plans for 1958. First, a new exhibit titled "How We Breathe" will be ready for bookings after January 1, 1958. This exhibit will present a three dimensional model for the organs involved in breathing—the nose, pharynx, larynx, bronchial tubes, and lungs. Other features include actual preserved human lungs; a unit to demonstrate the mechanism of breathing and the part played by the diaphram and rib cage, and a section showing the exchange of oxygen from the lungs to the blood and carbon dioxide from the blood to the lungs.

Two other exhibits also are well along in the planning stages for next year: (1) the brain and nervous system, featuring a human brain embedded in plastic, and (2) the endocrine system. Further details will be announced later.

Finally, small editions of the popular "Life Begins" exhibit are being built, incorporating most of the information in the large exhibit but displaying only one fetus embedded in plastic. Other fetuses in varying stages of development will be shown pictorially. This type of exhibit is extremely lightweight and should prove most attractive to those medical societies far away from Chicago.

A.M.A. Plans Two "Nomenclature" Institutes in '58

So popular have the Nomenclature Institutes been that the American Medical Association again plans to sponsor two more of these short courses during 1958. The first will be conducted March 31 to April 2 at Tulsa, Oklahoma. The second will be held in July in Boston. These three-day meetings are planned by the A.M.A. as a special service to medical record librarians and others working with the **Standard Nomenclature of Diseases and Operations** in the hospital, clinic or doctor's office. Queries should be sent to the A.M.A.

First Come, First Served

It's time for medical societies to begin planning for 1958 county and state fairs. The A.M.A. Bureau of Exhibits urges all medical societies to arrange for bookings of specific health exhibits as soon as possible. A number of commitments for some of the more popular exhibits have already been made.

Wintertime Fun

How to live sensibly and still have a good time in cold weather is the way of life outlined in a new series of radio transcriptions the A.M.A.'s Bureau of Health Education will have available for use by medical societies early in December. In the 13-program series "The Picture of Health," brief dramatizations of typical family life are presented. Subjects covered include: general winter exposures; snow and ice hazards for pedestrians; frostbite and chilblains; skiing hazards; diet; driving; household procedures (such as temperature and moisture in the room). Dr. W. W. Bolton, Bureau associate director, serves as medical consultant.

1957 Survey of County Medical Societies

Replies to the questionnaires sent to county medical societies concerning their activities and programs have been tabulated and published in booklet form by the A.M.A.'s Council on Medical Service. The booklet—"1957 Nationwide Survey on County Medical Society Activities—contains information on types of county medical society programs (such as emergency call systems or grievance committees), fee schedules, life insurance, attendance at meetings and dues. Copies will be sent to all county and state medical societies. Additional copies may be secured from the Council.

Trans-Atlantic Conference on Cancer Chemotherapy

Scientists in the United States and Great Britain will be joined by the new underseas cable on Wednesday, December 4, to exchange information on a vital frontier in research, cancer chemotherapy. It will be the second trans-Atlantic medical conference in history.

Three world medical centers will be linked—Philadelphia, where the American Medical Association will be convened in its eleventh annual Clinical Meeting; London, where a special panel will meet in Barnes Hall of the Royal Society of Medicine, and Bethesda, Maryland, where the program will be heard by scientists at the National Institutes of Health.

The hour-and-a-quarter conference on "Advances in the Chemotherapy of Cancer" will be sponsored by the A.M.A. and the Royal Society of Medicine in cooperation with Smith, Kline & French Laboratories.

In Philadelphia, arrangements have been made so that physicians attending the Clinical Meeting can hear the discussions starting at 3 p.m. EST over a special high-fidelity system in the Grand Ballroom of Convention Hall, scene of the winter meeting's scientific programs. Similar plans are being made in London and Bethesda.

Smith, Kline & French said these trans-Atlantic conferences are part of its program to foster international relations in the medical profession. Such activities in all professions and walks of life were urged by President Eisenhower last year in his "people-to-people" address.

The Academy of Psychosomatic Medicine

The following officers were elected at the fourth annual meeting of The Academy of Psychosomatic Medicine held October 17-19, 1957 at the Morrison Hotel in Chicago:

President—Dr. Bernard B. Raginsky, Montreal, Quebec, Canada.

Vice President — Dr. Lester L. Coleman, New York City.

Secretary—Dr. Wilfred Dorfman, Brooklyn, New York.

Treasurer—Dr. George F. Sutherland, Baltimore, Maryland.

Historian—Dr. Maury Sanger, Brooklyn, New York.

President-Elect—Dr. William S. Kroger, Chicago, Illinois.

American Roentgen Ray Society

At the fifty-eighth annual meeting of the American Roentgen Ray Society, held in Washington, D. C., October 1-4, the following chief officers were elected to serve through 1957-1958:

President-Elect—Barton R. Young, M.D., Germantown, Pennsylvania.

Secretary—C. Allen Good, M.D., Rochester, Minnesota.

Treasurer—Robert K. Arbuckle, M.D., Oakland, California. re-elected.

Chairman, Executive Council — Wilbur Bailey, M.D., Los Angeles, California.

Wendell G. Scott, M.D., St. Louis, Missouri, assumed the office of the presidency upon the first session of the Society's meeting, October 1.

The 1958 meeting will be held in Washington, D. C., September 27—October 3, in the Shoreham Hotel.

Pan American Sanitary Bureau

Nuclear radiation in all its forms is generally harmful to living organisms, and the radioactive contamination of any inhabited area presents a major public health problem which must be solved, if nuclear energy is to be fully utilized. All medical and public health workers must, therefore, be trained to meet the new demands made on them, according to the World Health Organization's Expert Committee on Professional and Technical Education of Medical and Auxiliary Personnel.

During its fourth session just held in Geneva under the chairmanship of Sir Ernest Rock of Carling, London, the Committee drew up a training schedule for all categories of public health personnel. This will bring hospital administrators, industrial hygiene workers, sanitary and hydraulic engineers, veterinary health officers, mental health specialists, and public health nurses back to school for periods ranging from one day to several weeks to learn how to protect the public against radiation. The same type of training is envisaged for public health workers now undergoing their basic studies.

Fundamentally, the Committee stated, the approach must be one of prevention through the limitation or elimination of exposure, since, at the present time, there is no entirely satisfactory method for alleviating the effects of radiation injury once it has been sustained, except in certain late cases through plastic surgery.

American Foundation for Allergic Diseases

Announcement of post-doctoral fellowships in research and clinical allergy for two years each has been made by the American Foundation for Allergic Diseases.

Stipend: first year, $4,500; second year, $4,750; laboratory expenses for the two-year period, $750.

Candidates must be graduates of approved medical schools and must have completed one or two years of graduate training requiring as a preliminary to certification by the Board of Internal Medicine or Pediatrics; they are to divide their time between research and clinical training and, in the second year, teaching. This training will be credited toward the Sub-specialty in Allergy by the Board of Internal Medicine and the Board of Pediatrics.

Requests for applications should be sent directly to one of the following in whose field the candidate would like to work: Dr. Colin M. MacLeod, Professor of Research Medicine, University of Pennsylvania, 820 Maloney Clinic, 36th and Spruce Streets, Philadelphia 4, Pennsylvania; Dr. Herman N. Eisen, Professor of Medicine (Dermatology), Washington University School of Medicine, 600 South Kingshighway, Saint Louis 10, Missouri.

American College of Chest Physicians

The Fifth International Congress on Diseases of the Chest, sponsored by the American College of Chest Physicians, will be held in Tokyo, Japan, September 7-11, 1958. The Congress will be presented under the patronage of the Government of Japan and the Japan Science Council. The Congress has been endorsed by the Japan Medical Association.

Eminent scientists from countries throughout the world will participate in discussions on a variety of subjects. The proceedings will be simultaneously interpreted into the three official languages for the Congress—Japanese, French, and English.

The registration fee for each physician attending the Congress is $25.00 (U. S. currency) and $10.00 for each family member accompanying the physician.

For additional information write: Mr. Murray Kornfeld, Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

U. S. Atomic Energy Commission

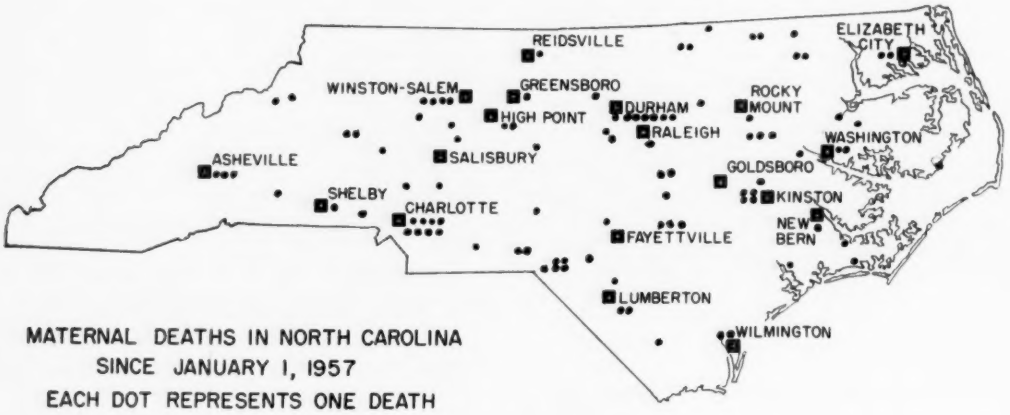
In order to help speed up the peaceful uses of nuclear energy throughout the world, the Atomic Energy Commission is participating in and supporting conferences which bring together in the United States groups of leading scientists from friendly nations for topical discussions on specialized atomic energy subjects.

This is the Atomic Energy Commission's response to a need, expressed by many scientists, for an opportunity to discuss the many unclassified problems and developments in atomic energy which cannot be taken up in the broad Geneva-type conference.

Not only will American scientists benefit from the exchange of ideas on scientific advances, but it is hoped that these discussions will do much to lower the barriers which impede the interchange of information among friendly powers.

These conferences generally will be sponsored by private institutions in this country. They will cover various aspects of physics, chemistry, biology, medicine, and other sciences relating to nuclear energy.

The Fifth International Conference on Low Temperature Physics and Chemistry, held at the University of Wisconsin in August, and the International Conference on Neutron Physics and Chemistry, held at Columbia University in September, were among the first meetings in which the AEC took part and supported.



MATERNAL DEATHS IN NORTH CAROLINA
SINCE JANUARY 1, 1957
EACH DOT REPRESENTS ONE DEATH

The Month in Washington

Several months in advance of the return of the Eighty-fifth Congress for its election-year second session, influential figures in the field of health in both the executive branch of the government and in Congress were being heard with regard to what 1958 has in store for the medical profession.

Because of the roles they play in the Capital, their views are worth more than passing notice. One is the chairman of the important health appropriations subcommittee of the House, Rep. John Fogarty (D.,R.I.). He used as a forum for his prophecies the annual convention of the American Hospital Association.

Other prognostications came from Dr. Aims C. McGuinness, special assistant for health and medical affairs to Secretary Folsom of the Department of Health, Education, and Welfare. Dr. McGuinness spoke out at a dedication ceremony of a new chronic disease and rehabilitation facility in Maine.

Mr. Fogarty places at the top of his predictions some action on federal construction aid to medical schools. The Rhode Island Democrat has his own bill on the subject, although there are others pending. Comments Mr. Fogarty: " . . . the shortage of health education facilities today is probably the most serious bottleneck in our whole medical system . . . These schools . . . fall far short of accomodating the fully qualified and competent young men and women in America who are anxious to train and qualify in medical, dental, and public health fields."

The record of the past several years has shown that no member of the House is listened to more carefully when it comes to health than Mr. Fogarty. His philosophy in the health field is worth noting: "It is now generally accepted that the health of our people is a major national resource and that the government, therefore, has a direct responsibility for the health of everyone."

Dr. McGuinness also spoke out strongly for federal aid to medical schools. Failure to meet the needs of the schools, he told his audience, would be "the worst kind of economy." He feels that the administration proposal for $225 million in construction grants would bring classrooms and research laboratories "much closer to current and projected needs."

While neither man had any specific legislative proposals to make in the field, both foresee a growing role for hospitals in the practice of medicine. Dr. McGuinness put it this way: "General hospitals must broaden their services and achieve greater coordination. The term 'hospital care' should include not only bed care but diagnostic service as well as service to ambulatory patients."

Mr. Fogarty, looking ahead 25 years, said it was safe to predict that virtually every general hospital in the nation will be providing at least as much preventive service as curative service. "You are, in fact, moving closer each moment to the day when hospitals will be the focal point of health services for all of us, throughout our entire lives."

The same day that Mr. Fogarty was urging the hospitals to use the basic Hill-Burton hospital construction program to meet future health needs, the AHA House of Delegates approved a set of legislative proposals to present to the next session.

They would accomplish the following: (1) extend the act for five years beyond June, 1959, (2) authorize matching Hill-Burton funds for renovation and repairs of hospital plants, (3) set up loan authority so that hospitals not desiring grant money could borrow construction and renovation funds at very low interest rates (from 1½ to 2 per cent). The House also urged a grants program to hospitals with nursing schools and to other nurse institutions for professional education, exclusive of construction grants.

* * *

Notes

One committee of Congress knows months in advance just exactly what it plans to do the day Congress reconvenes. The tax-writing House Ways and Means Committee has set hearings starting January 7 on possible tax reductions next year.

Included on the agenda will be testimony from various organizations on the Jenkins-

From the Washington Office of the American Medical Association.

Keogh bills for allowing tax deferments for money paid into retirement plans. The American Thrift Assembly, which is backed by the American Medical Association and other professional and business groups, plans to be heard at some time during the 30 days of hearings.

* * *

Veterans Administrator Harvey Higley believes that the public is losing interest in the veteran and his problems, and that some doctors no longer hesitate to attack medical care for veterans, particularly those with non-service-connected disabilities. Mr. Higley spoke at the annual American Legion convention.

* * *

Health directors of 21 American republics, holding their annual Pan American Sanitary Organization meetings here this fall, voted a $3 million budget for the Pan American Sanitary Bureau's 160-odd health projects for next year.

Healing of Donor Sites Speeded With Furacin

Donor sites from which skin grafts are removed with a dermatome offer excellent opportunities for the study of wound healing. Such a study has recently been reported by J. V. Jeffords, M.D., and Robert F. Hagerty, M.D., from the Department of Surgery of the Medical College of South Carolina, Charleston. Color photograph records of the healing process add to the value of their data.

The surgeons were interested in making a quantitative and qualitative comparison of the effects of Furacin Soluble Dressing and an aseptic technique, using petrolatum-impregnated fine mesh gauze on the healing of the donor sites. They found much better results with Furacin, the percentage of epithelization being higher in the Furacin-treated sites. This was probably due in part to suppression of secondary bacterial infection.

In 38 patients, 50 donor sites each were dressed half with gauze (unbleached muslin) impregnated with Furacin Soluble Dressing (Eaton) and half with petrolatum gauze. The average percentage of epithelization of sites dressed with Furacin gauze was 90.2 per cent as compared with 80.3 per cent with the control gauze. The frequency of adherence of the epithelizing surface of the wound to the fine mesh gauze impregnated with Furacin Soluable Dressing was less than with petrolatum. No evidence of sensitization to Furacin was noted in this study.

(Jeffords, J. V., and Hagerty, R. F.: The healing of donor sites. Ann. Surg. 145:169 (Feb.) 1957.)

BOOK REVIEWS

New Research Techniques of Neuroanatomy: A Symposium Sponsored by the National Multiple Sclerosis Society. Edited by William F. Windle. 108 pages, with 25 illustrations. Price, $4.75. Springfield, Illinois: Charles C Thomas, Publisher, 1957.

This book records the talks given at a symposium sponsored by the National Multiple Sclerosis Society. There are nine contributors. The methods discussed include electron microscopy, two modifications of older silver impregnation methods, tissue culture (hardly a new technique), blood flow studied by radio-autography, and some histo-chemical methods. For the most part, the details of the methods are discussed more extensively than the results. The latter are available elsewhere in better form and greater clarity. These methods appear to hold promise for the future, but the meaning of much of the material is not revealed in this presentation. The use of words such as "adielectronic," "maientic," and "post-osmicated" does not help the reader.

Methods in Surgical Pathology. By Henry A. Teloh, M.D. 127 pages. Price, $4.75. Springfield, Illinois: Charles C Thomas, Publisher, 1957.

This handbook contains chapters devoted to operating room procedures, gross examination, frozen section, records, culture methods, prognosis, and a procedure for various organs that are presented to the laboratory for analysis. The appendix includes protocols of gross and microscopic examination followed by diagnosis.

The large print and directive style should make the book a convenient and valuable guide, especially for residents. Although the presentation by necessity is detailed, the lengthy discussion and repetitious form make for tedious reading. Emphasis is properly placed on prognosis and the need to quantitate pathologic change.

Anesthesiology and Related Problems. Edited by Otto V. St. Whitelock. 181 pages. Price, $4.00. Annals of the New York Academy of Sciences, Vol. 66, Art. 4, pages 841-1022, 1957.

Of interest primarily to the surgeon and to the anesthesiologist, this symposium is given by 26 authorities. The 16 articles fall into four parts: geriatric anesthesia, controlled respiration, fluid and electrolyte balance, and hypotension.

Intriguing subjects, such as mechanical respirators and the effects of pressure breathing on the pulmonary circulation, are discussed. The question of possible harmful effects of respiratory alkalosis due to manual hyperventilation is dealt with in some detail. Dr. Harris' clear discussion of problems in fluid and electrolyte therapy in pediatric

surgery is of interest to anyone who treats hospitalized children. The article by Dr. Burstein on adrenocortical insufficiency presents examples of proper and improper preparation of the steroid-treated patient. Zweifach and Hershey, in their article on protective mechanisms in shock, leave the reader hanging in mid air, as no special conclusions are drawn. And who can rightly draw many definite conclusions on this subject, except that there is a need for further study? Dr. Barber presents a practical review of nutritional and hematologic problems in the geriatric patient.

Nearly every physician would find this symposium worth-while reading. Many anesthesiologists would want to add it to their bookshelves.

The Bases of Treatment. By Neuton S. Stern, M.D., and Thomas N. Stern. 176 pages. Price, $4.75. Springfield, Illinois: Charles C Thomas, Publisher, 1957.

This book, as stated in the introduction, is not intended as a materia medica, with specific remedies for various diseases, but is rather a somewhat philosophic discussion of the general principles upon which therapy is based. Part I begins with an excellent chapter on the importance of confidence in the physician, and sound advice on how to win and deserve the confidence of the patient and his family. Other chapters deal with diagnosis as a basis of treatment; disease as a dynamic process; and disease as a disturbed physiologic process. Part II, Care of the Patient, discusses fluid and electrolyte balance, diet, the comfort of the patient, and philosophic considerations in the use of drugs. Part III, Special Cases in Therapy, takes up prevention of disease, iatrogenic disease, and psychotherapy.

The book should be helpful to students and practitioners as presenting fundamental principles of treatment, which should hold good through the years. It is not intended as a volume on current therapy.

The Medical Interview: A Study of Clinically Significant Interpersonal Relations. By Ainslie Meares, M.B.B.S., B. Agr. Sc., D.P.M. 117 pages. Price, $3.50. Springfield, Illinois: Charles C Thomas, Publisher, 1957

The author, a practicing psychiatrist, states in the introduction that "The medical interview is distinct from medical history-taking on the one hand, and the psychiatric interview on the other. It refers to the discussion which takes place when it is some problem rather than a symptom which brings the patient to consultation." He then discusses the motives that send patients for advice; the importance of rapport between doctor and patient; ways of encouraging patients to express their fears and conflicts; and the power of suggestion, rightly used.

The aim of the book, as stated on the cover, is commendable: "To help patients by the simple procedure of talking to them." Unfortunately, a formidable language barrier is apt to discourage the reader at the beginning. There is much good advice in the book, but it has to be dug out from a tangled mass of words, too many of them unnecessarily long and technical.

The Care of The Expectant Mother. By Josephine Barnes, 270 pages. Price, $7.50. New York: The Philosophical Library, 1957.

This monograph consists of three parts: first, a short section on normal anatomy and physiology of pregnancy; second, nine chapters on abnormal gestation; and finally, ten chapters concerned with diseases complicating pregnancy. The latter two sections are a veritable Cook's tour of pregnancy complications, a situation that of necessity limits detailed description of disease entities or management in a volume of this size.

The text is considered inadequate as a synopsis of obstetrics and too limited in its scope to serve as a textbook for medical students. Perhaps the most legitimate application of this volume is in nursing or midwife training, where comprehensive coverage of the various topics discussed is not required. The text is considered clear and accurate and the management of obstetric problems is conservative. Illustrations are adequate and the format attractive.

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Application

FOR SPACE IN THE SCIENTIFIC EXHIBIT

1958 Annual Meeting — Medical Society of the State of North Carolina

Asheville City Auditorium — **Asheville, N. C.** — **May 4, 5, 6, 7, 1958**

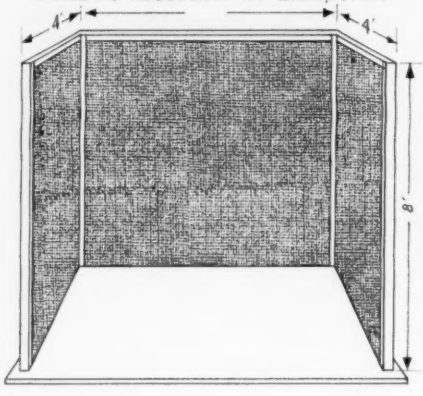
Fill Out and Mail to:

EVERETT I. BUGG, M.D., Chairman
Committee on Scientific Exhibits
Broad and Englewood Streets
Durham, N. C.

(Applications for space should be received before January 15, 1958)

Dimensions and structure of Medical Society of the State of North Carolina Scientific booth are shown in accompanying illustration.

SPACE AS RESERVED BY EXHIBITOR



1. Title of Exhibit: .....
2. Description or nature of exhibit: (Attach brief description to this blank).
3. Will you require shelf space? .....
4. Give approximate amount of back wall space needed. (Included in total space is two side walls of four feet in depth) .....
5. Name of institution co-operating in the exhibit (if desired) .....
6. Name of exhibitor: .....
7. Title: .....
8. Address ..... (Street & No. ..... (City)
   (a) First Associate
   (b) Second Associate

The Medical Society of the State of North Carolina will provide without cost to the exhibitor the following: Exhibit space, sign for booth and current; provided all items are approved in advance by the committee.

Cost of transporting exhibits to and from the meeting must be borne by the individual exhibitor as well as costs of cards, signs, etc., which are a part of the exhibit.

View boxes, furniture, decorations, etc., may be rented, if desired, by applying directly to Howard Hoover Display Company, P.O. Box 5375, Station E., Atlanta 7, Ga., who supply equipment for the annual Medical Society of the State of North Carolina meeting.

In Memoriam

CLARENCE N. PEELER, M.D.

WHEREAS, By the death of Doctor C. N. Peeler on August 28, 1957, the Mecklenburg County Medical Society was deprived of one of its oldest members and one of its past presidents; and,

WHEREAS, in his long and distinguished career, he was always a faithful attendant at the meetings of the Society and a frequent contributor to its proceedings; and,

WHEREAS, In his professional and personal life he consistently reflected the finest traditions of medicine; and,

WHEREAS, Not only because of the above attributes but because of his innate thoughtfulness, kindliness and tolerance he was one of the most beloved and respected members of this Society;

Be It Therefore Resolved That we extend to the family our profound regret in our mutual loss but at the same time being mindful of a happier side, *viz.*, that this is a better medical society, his community a better community, his Church a better church, his beloved Wake Forest a better college, and his state a better state because of his sojourn here;

And Be It Further Resolved That a copy of these resolutions be incorporated in the permanent files of the Society and a copy be forwarded to his family.

JOHN WATTS FARTHING, M.D., F.A.C.S.

Wilmington and Eastern North Carolina, along with the medical profession, suffered a tragic loss upon the death of Dr. John Watts Farthing, July 27, 1957. Dr. Farthing, only 48 years of age, had been in declining health for several months preceding his unexpected death from cardiorespiratory complications.

Dr. Farthing was born in Pittsboro, North Carolina, March 3, 1909, the son of Dr. and Mrs. L. E. Farthing. He grew up in Wilmington, where his father was a prominent physician for many years. Following graduation from New Hanover High School, he matriculated at the University of North Carolina and, upon graduation in 1929, entered the Medical School of the University of Pennsylvania. An honor student, he graduated in 1933, served as an intern in the Hospital of the University of Pennsylvania from 1933-1935, and then advanced to a fellowship in surgery at the Mayo Clinic. Upon the completion of his surgical training, with an M.S. in Surgery, 1938, he returned to Wilmington and began the practice of general surgery.

A successful surgical practice developed and continuously progressed up to his retirement in January, 1957, because of failing health. He felt that physically he was no longer able to give his patients the untiring and unexcelled care which had characterized his entire surgical career.

Fellowship in the American College of Surgeons was achieved in 1942; membership in the New Hanover County Medical Society, North Carolina, American Medical Association, the Southeastern Surgical Congress, the North Carolina Surgical Association, and the Society of Railroad Surgeons was bestowed upon him, and valuable, untiring service to them continued through the years. He was an attending surgeon, James Walker Memorial Hospital, former chief of staff, and consulting surgeon, Community Hospital, Wilmington.

Dr. Farthing was a deacon in the First Presbyterian Church of Wilmington, a 32nd Degree Mason, an active member of the Civitan Club, and was active in numerous other civic organizations. His was an active role in the community life of this area.

Now therefore it is moved, seconded, and adopted that this resolution and expression of our bereavement and loss at the passing of our colleague and friend be sent to the family of the late Dr. John Watts Farthing. Furthermore, this resolution shall be entered into the minutes of this Society, with copies to be transmitted to the Medical Society of the State of North Carolina and the American College of Surgeons.

Adopted this 18th day of September, 1957.

S. E. Warshauer, M.D.
E. J. Wells, M.D.
New Hanover County Medical Society

ANNIE THOMPSON SMITH, M.D.

Dr. Annie Thompson Smith was born in Evington, Virginia, on May 14, 1894. Her family moved to Durham about 1901. She attended the Durham City Schools and graduated from the Durham High School in 1912. She graduated from Trinity College, Durham, North Carolina, in the Class of 1917, with a B.A. degree. She received her M.A. degree in 1918. She took her first two years of medicine at the University of North Carolina Medical School and the last two years at the University of Illinois, from which she was graduated in 1923. She spent two years as an intern at St. Francis' Hospital, Evanston, Illinois, and several summers at the University of Michigan, Ann Arbor, and at Washington University, St. Louis, doing postgraduate work. She was a resident at the West Philadelphia Woman's Hospital in Philadelphia for six months before coming to Durham to practice medicine in April, 1926. For several summers after coming to Durham, she attended Post-Graduate Hospital in New York. After beginning her practice in Durham in April, 1926, she carried on an active general practice until a few months prior to her death.

She was interested in all sorts of civic activities. She was a charter member of the Business and Professional Women's Club. She was a charter member of the Altrusa Club and helped organize it. She was active in the American Association of University Women. She was a member of the Durham-

Orange County Medical Society and of the Academy of General Practice. At one time she was very active in Girl Scouting. She was an active member of the Presbyterian Church. She was active in the charity service at Lincoln and at Watts Hospitals. She did outstanding service in the well-baby clinic at Lincoln Hospital and took a sincere interest in the parents at the clinic. As the first woman to practice medicine in Durham, she was active in her chosen profession and carried on a large private practice.

To say that Annie Thompson Smith was a good doctor does not begin to express what one would like to say about her. She was well informed. She gave her patients her best, and she never hesitated to call for consultation when she felt that she needed it. She gave freely of her time and service and spent hours in free clinics without thought of recompense. Her patients loved her. She read, she loved music, and she was tremendously interested in the humanities. She believed that woman should hold a dignified place in her profession. It is doubtful if anyone ever heard her say an unkind word about any person. She was as free from prejudice and bias as any person could be. She believed in the Hippocratic Oath and followed it closely. Her patients and her friends came first. There was nothing selfish in her makeup. When her friends were right, she praised them; when they were wrong, she told them.

She did not write a biographical sketch of her last illness. There will be no book to celebrate the last battle that she fought, but she faced this battle with a courage that could not have been excelled. The fact that she lived by the Hippocratic Oath is correct, but another man that she followed more closely than she did Hippocrates was a man called Christ. She lived as He would have wanted her to live.

J. Kempton Jones, M.D.
Secretary, Durham-Orange
County Medical Society

WILLIAM T. SHAVER, M.D.

On July 16, 1957, death came to our friend and colleague, Dr. William T. Shaver of Albemarle. The medical profession and his community suffered a severe loss in the death of Dr. Shaver, which occurred as a result of a coronary occlusion at his home.

William Trantham Shaver was born July 30, 1893, in Salisbury, North Carolina, and received his earlier schooling in the Salisbury schools. He attended the University of North Carolina and was graduated from the University of Maryland School of Medicine in 1919. He completed his surgical residency at Maryland General Hospital in Baltimore. He began his practice of surgery in Badin, North Carolina, in 1920, later moving to Albemarle in 1926, where he established a surgical clinic. For 22 years he served as medical director of the Yadkin Hospital, in addition to carrying on his practice of surgery.

He was married to Miss Ada Worsham, and from this marriage there was one child, a daughter, Mrs. Laura Maie Shaver Pettee, of Wilmington, North Carolina.

Honors and responsibilities rested lightly on the shoulders of this physician, and he carried both with great dignity and with pride. He will long be remembered by many for his work, especially with the youth of this community. His service as county chairman of the Morehead Scholarship Foundation and his interest and participation in the American Legion Junior Baseball program are only two of the facets of youth that shine brighter as a result of his life.

The medical profession was considerably advanced by his wise counsel and guidance. He was a past president of the Stanly County Medical Society, a past president of the Seventh District Medical Society, and was chief of staff of the Stanly County Hospital in 1953. He was firm in his decisions and uncompromising in his duty; but, withal, he had a rare sense of humor which stood him in good stead whenever difficult decisions presented themselves.

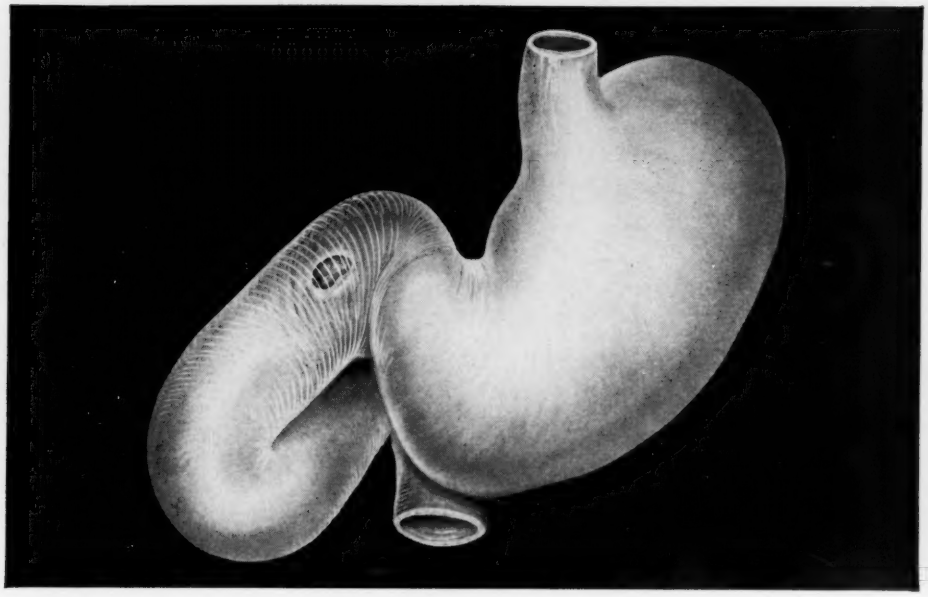
In the death of Dr. Shaver, the Stanly County Medical Society, and the community in which he served lost one of the real doctors of the "old school." He was both a scholar and a true gentleman. Of him it might well be said: "His life was gentle, and the elements so mixed in him that Nature might stand up and say to all the world, 'This was a man.'"

In his memory, **Be It Resolved** that we, as a society, extend our deep and abiding sympathy to his widow, Mrs. Ada Worsham Shaver, and his daughter, Mrs. Laura Maie Shaver Pettee.

BE IT FURTHER RESOLVED, that a copy of this rememberance be given to the members of his immediate family, a copy sent to the NORTH CAROLINA MEDICAL JOURNAL, and a copy incorporated into the proceedings of this Society.

Resolutions Committee
Stanly County Medical Society
H. L. Murray, M. D., Chairman
W. H. Freeman, M.D.
Edward S. Bivens, M.D.

CONFIRMED THERAPEUTIC UTILITY



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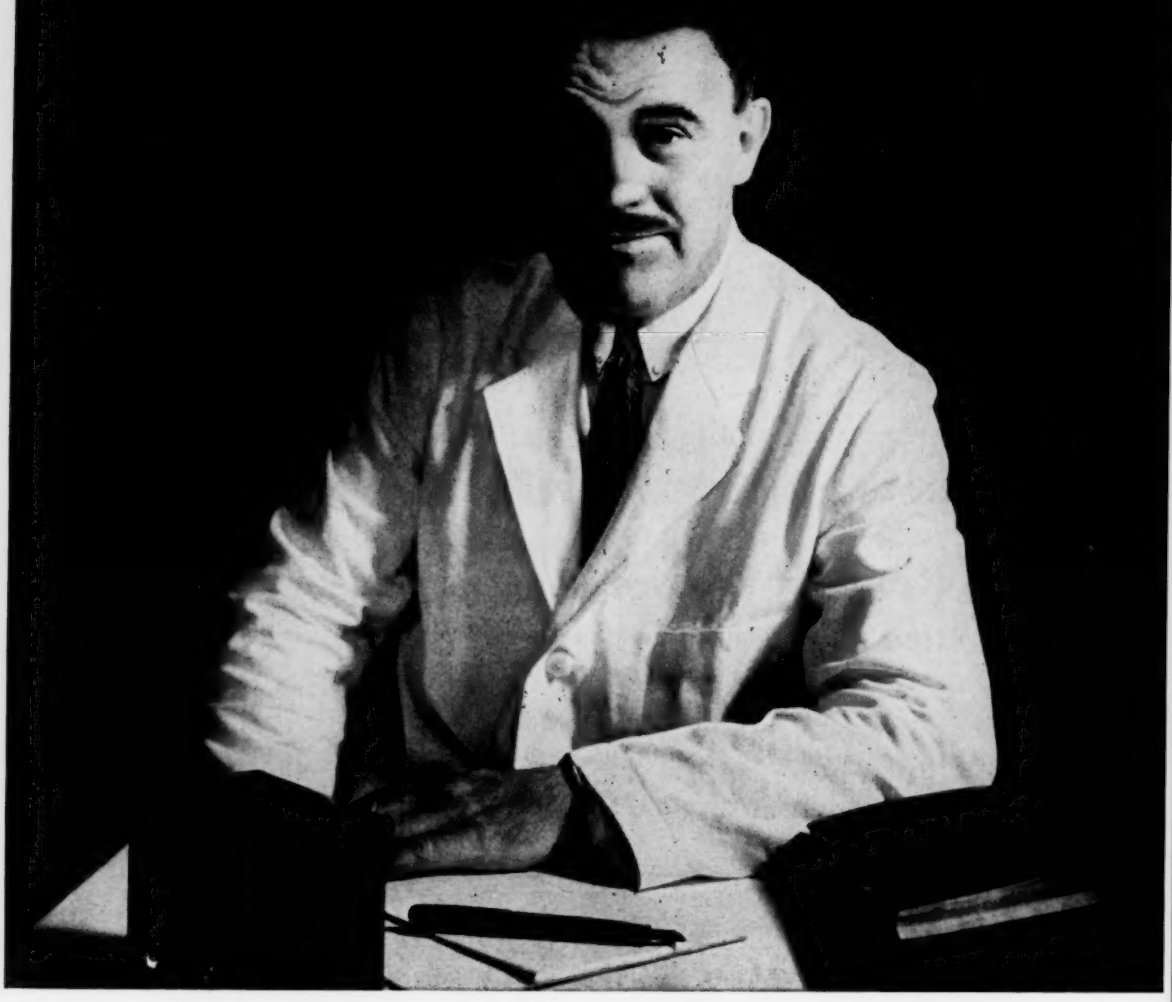
*Lichstein, J.; Morehouse, M. G., and Osmon, K. L.: Pro-Banthine in the Treatment of Peptic Ulcer. A Clinical Evaluation with Gastric Secretory, Motility and Gastroscopic Studies. Report of 60 Cases, Am. J. M. Sc. *232*:156 (Aug.) 1956.

SEARLE

KEY MAN AGAINST CANCER



YOUR OFFICE, DOCTOR, is the "cancer detection center" which we urge all adults to visit once a year, and where early diagnosis of cancer can help save many thousands of lives. It is upon you that we largely rely for the carrying out of many aspects of our education, research and service programs. As members of our Boards of Directors — on the National, Division and Unit levels — it is your thinking and your guidance which are such vital factors in creating and executing our policies and programs.

You, of course, are concerned with all the ills affecting the human body. The American Cancer Society deals specifically with cancer. But our mutual concern — the tie that binds us inextricably—is the saving of human lives. Through your efforts, we may soon say—"one out of every two cancer patients is being saved." Indeed, with your help, cancer will one day no longer be a major threat.

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ACHROSTATIN V combines ACHROMYCIN† V . . . the new rapid-acting oral form of ACHROMYCIN† Tetracycline . . . noted for its outstanding effectiveness against more than 50 different infections . . . and NYSTATIN . . . the antifungal specific. ACHROSTATIN V provides particularly effective therapy for those patients who are prone to monilial overgrowth during a protracted course of antibiotic treatment.

supplied:

ACHROSTATIN V CAPSULES contain 250 mg. tetracycline HCl equivalent (phosphate-buffered) and 250,000 units Nystatin.

dosage:

Basic oral dosage (6-7 mg. per lb. body weight per day) in the average adult is 4 capsules of ACHROSTATIN V per day, equivalent to 1 Gm. of ACHROMYCIN V.

*Trademark
†Reg. U. S. Pat. Off.

Lederle LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, N. Y.

GLENWOOD PARK SANITARIUM

Founded by
W. C. ASHWORTH,
M. D.
1904

GREENSBORO,
North
Carolina

Established in 1904 and continuously operated since that date for the medical treatment of drug and alcoholic addictions. Located in an attractive suburb of Greensboro where privacy and pleasant surrounding are to be found.

WORTH WILLIAMS, *Business Manager* R. M. BUIE, JR., *Medical Director*

Address: GLENWOOD PARK SANITARIUM, Greensboro, N. C.

Telephone: 2-0614

Thirst, too, seeks quality

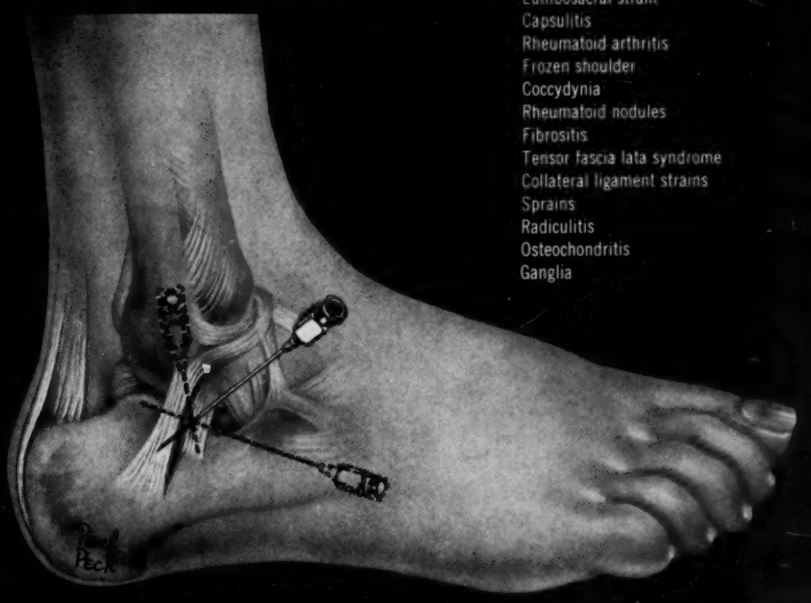
NEW **HYDELTRA®-T.B.A.**

(Prednisolone *tertiary*-butylacetate, Merck)

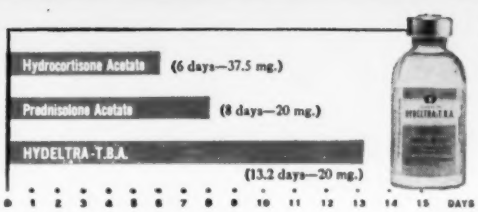
for relief that lasts—longer

in *SPRAINS*—
reduces tenderness,
swelling and
limitation of motion

- Osteoarthritis
- Acute gouty arthritis
- Bursitis
- Tendinitis
- Trigger finger
- Peritendinitis
- Trigger points
- Tennis elbow
- Lumbosacral strain
- Capsulitis
- Rheumatoid arthritis
- Frozen shoulder
- Coccydynia
- Rheumatoid nodules
- Fibrositis
- Tensor fascia lata syndrome
- Collateral ligament strains
- Sprains
- Radiculitis
- Osteochondritis
- Ganglia



Anti-inflammatory effect lasts longer than that provided by any other steroid ester


Hydrocortisone Acetate
(6 days—37.5 mg.)
Prednisolone Acetate
(8 days—20 mg.)
HYDELTRA-T.B.A.
(13.2 days—20 mg.)
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 DAYS

Dosage: the usual intra-articular, intra-bursal or soft tissue dose ranges from 20 to 30 mg. depending on location and extent of pathology.

Supplied: Suspension 'HYDELTRA'-T.B.A.—20 mg./cc. of prednisolone *tertiary*-butylacetate, in 5-cc. vials.

MSD

MERCK SHARP & DOHME
DIVISION OF MERCK & CO., INC.
PHILADELPHIA 1, PA.

simple, well-tolerated routine for "sluggish" older patients

one tablet t.i.d.

DECHOLIN®

"therapeutic bile"

Establishes free drainage of biliary system—effectively combats bile stasis and improves intestinal function.

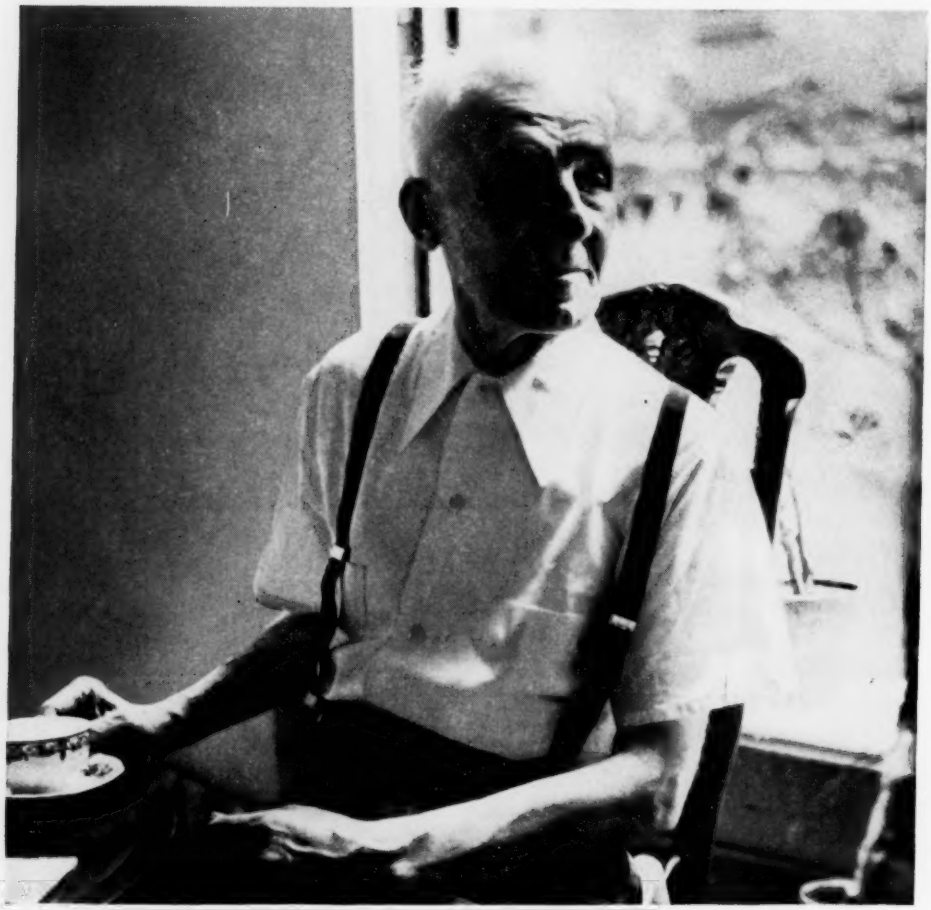
Corrects constipation without catharsis—copious, free-flowing bile overcomes tendency to hard, dry stools and provides the natural stimulant to peristalsis.

Relieves certain G.I. complaints—improved biliary and intestinal function enhance medical regimens in hepatobiliary disorders.

DECHOLIN Tablets: (dehydrocholic acid, AMES) 3¾ gr.

23787

AMES COMPANY, INC · ELKHART, INDIANA · Ames Company of Canada, Ltd., Toronto



The Upjohn Company announces a major corticosteroid improvement

minor chemical changes can mean major therapeutic improvements

Medrol*

The most efficient of all anti-inflammatory steroids

- Lower dosage (⅓ lower dosage than prednisolone)
- Better tolerated (less sodium retention, less gastric irritation)

Supplied: Tablets of 4 mg., in bottles of 30 and 100.

For complete information, consult your Upjohn representative, or write the Medical Department, The Upjohn Company, Kalamazoo, Michigan.

*TRADEMARK FOR METHYLPREDNISOLONE, UPJOHN

Upjohn

Prescription for Your Peace of Mind

Among the many worries of the Professional Man is the worry about what will happen if he becomes disabled by sickness or accident. Chances are his professional income stops; there's no boss to keep him on the payroll; no 30-day sick leave; no workmen's compensation. Financial disaster might face his family and himself.

Protection aganist that kind of disaster is the reason for Mutual of Omaha's PROFESSIONAL MEN'S PLAN of accident and health insurance. Protect yourself by enrolling now in this plan designed to meet the special problems of the Professional Man.

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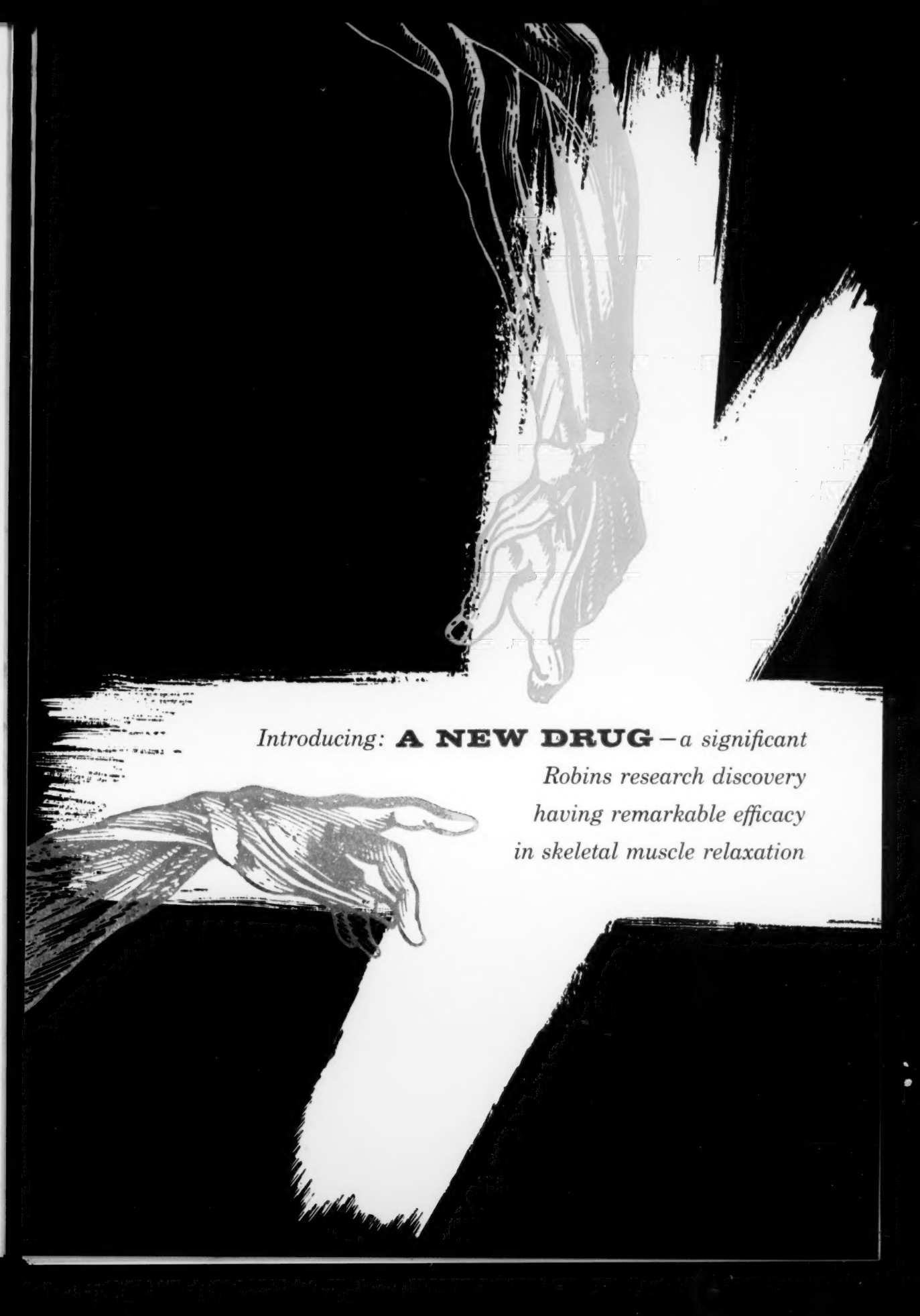

Introducing: **A NEW DRUG** — *a significant*
Robins research discovery
having remarkable efficacy
in skeletal muscle relaxation

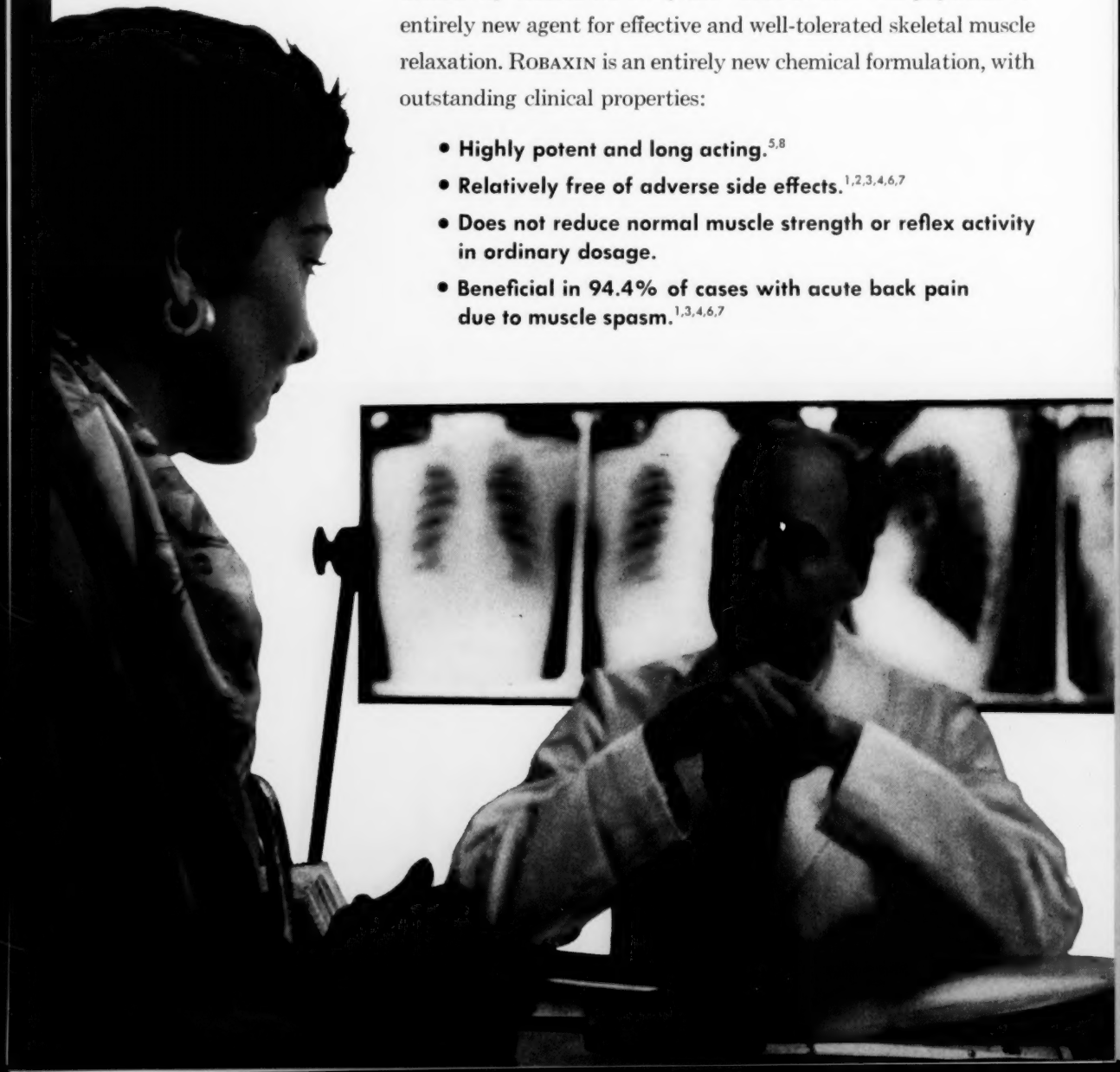
Significant **Robins** research discovery:

a highly efficient skeletal muscle relaxant

Ro

ROBAXIN – synthesized in the Robins Research Laboratories, and intensively studied for five years – introduces to the physician an entirely new agent for effective and well-tolerated skeletal muscle relaxation. ROBAXIN is an entirely new chemical formulation, with outstanding clinical properties:

- **Highly potent and long acting.**[5,8]
- **Relatively free of adverse side effects.**[1,2,3,4,6,7]
- **Does not reduce normal muscle strength or reflex activity in ordinary dosage.**
- **Beneficial in 94.4% of cases with acute back pain due to muscle spasm.**[1,3,4,6,7]



baxin®

(Methocarbamol Robins, U.S. Pat. No. 2770649)

Highly specific action

ROBAXIN is highly specific in its action on the internuncial neurons of the spinal cord – with inherently sustained repression of multisynaptic reflexes, but with no demonstrable effect on monosynaptic reflexes. It thus is useful in the control of skeletal muscle spasm, tremor and other manifestations of hyperactivity, as well as the pain incident to spasm, without impairing strength or normal neuromuscular function.

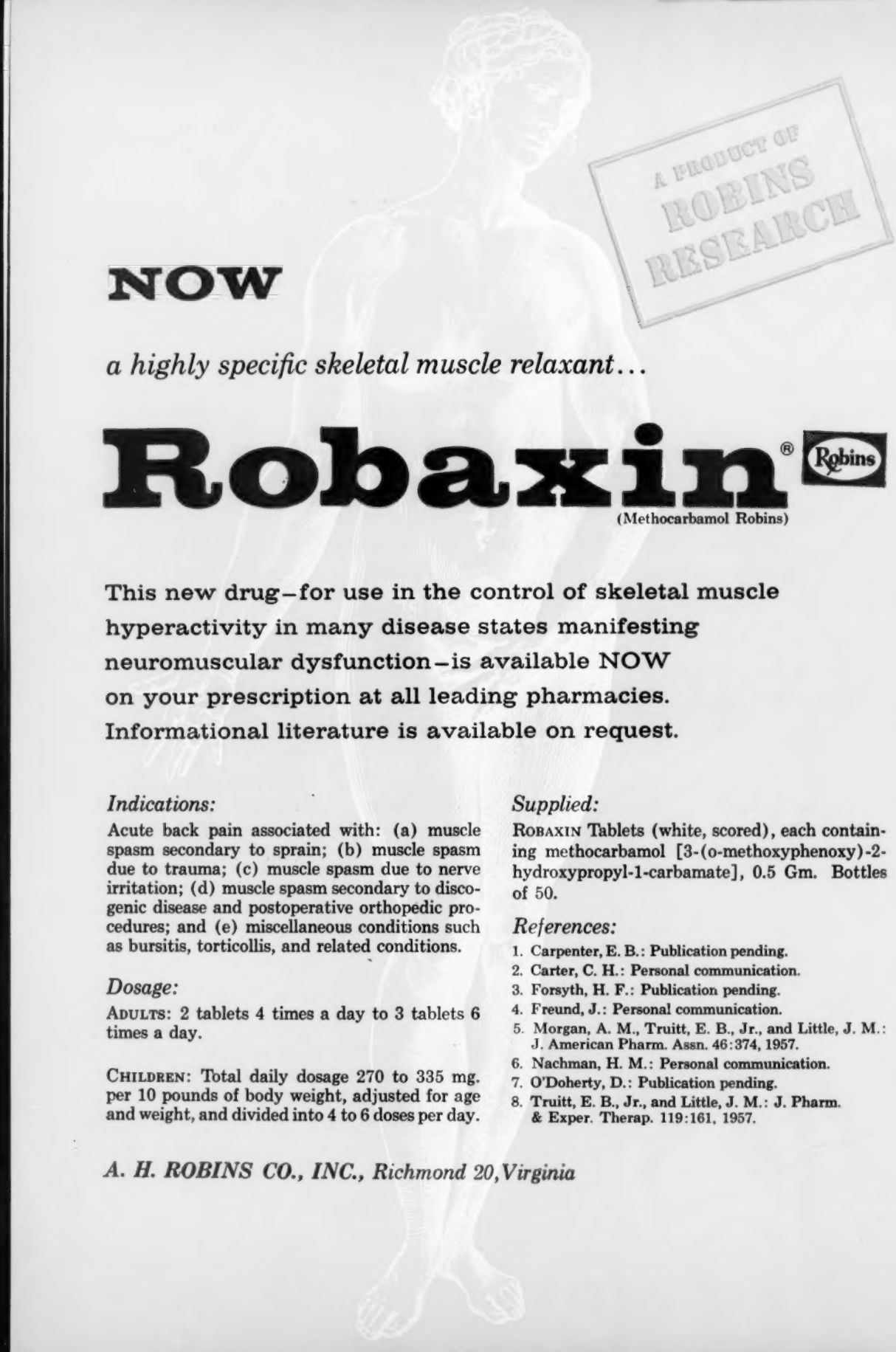
Beneficial in 94.4% of cases tested

When tested in 72 patients with acute back pain involving muscle spasm, ROBAXIN induced marked relief in 59, moderate relief in 6, and slight relief in 3 – or an over-all beneficial effect in 94.4%.[1,3,4,6,7] No side effects occurred in 64 of the patients, and only slight side effects in 8. In studies of 129 patients, moderate or negligible side effects occurred in only 6.2%.[1,2,3,4,6,7]

CLINICAL RESULTS WITH ROBAXIN IN ACUTE BACK PAIN[1,3,4,6,7]

Disease entity	No. of Cases	Duration of Treatment	Dose per day (divided)	Response				Side Effects
				Marked	Mod.	Slight	Neg.	
Acute back pain due to								
(a) Muscle spasm secondary to sprain	18	2-42 days	3-6 Gm.	17	1	0	0	None, 16; Dizziness, 1; Slight nausea, 1.
(b) Muscle spasm due to trauma	13	1-42 days	2-6 Gm.	8	1	3	1	None, 12; Nervousness, 1.
(c) Muscle spasm due to nerve irritation	5	4-240 days	2.25-6 Gm	4	1	0	0	None, 5.
(d) Muscle spasm secondary to discogenic disease and postoperative orthopedic procedures	30	2-28 days	1.5-9 Gm.	24	3	0	3	None, 25; Dizziness, 1; Lightheadedness, 2; Nausea, 2.*
Miscellaneous (bursitis, torticollis, etc.)	6	3-60 days	4-8 Gm.	6	0	0	0	None, 6.
TOTAL	72			59	6	3	4	

*Relieved on reduction of dose



NOW

a highly specific skeletal muscle relaxant...

Robaxin®

(Methocarbamol Robins)

This new drug—for use in the control of skeletal muscle hyperactivity in many disease states manifesting neuromuscular dysfunction—is available NOW on your prescription at all leading pharmacies. Informational literature is available on request.

Indications:

Acute back pain associated with: (a) muscle spasm secondary to sprain; (b) muscle spasm due to trauma; (c) muscle spasm due to nerve irritation; (d) muscle spasm secondary to discogenic disease and postoperative orthopedic procedures; and (e) miscellaneous conditions such as bursitis, torticollis, and related conditions.

Dosage:

ADULTS: 2 tablets 4 times a day to 3 tablets 6 times a day.

CHILDREN: Total daily dosage 270 to 335 mg. per 10 pounds of body weight, adjusted for age and weight, and divided into 4 to 6 doses per day.

Supplied:

ROBAXIN Tablets (white, scored), each containing methocarbamol [3-(o-methoxyphenoxy)-2-hydroxypropyl-1-carbamate], 0.5 Gm. Bottles of 50.

References:

1. Carpenter, E. B.: Publication pending.
2. Carter, C. H.: Personal communication.
3. Forsyth, H. F.: Publication pending.
4. Freund, J.: Personal communication.
5. Morgan, A. M., Truitt, E. B., Jr., and Little, J. M.: J. American Pharm. Assn. 46:374, 1957.
6. Nachman, H. M.: Personal communication.
7. O'Doherty, D.: Publication pending.
8. Truitt, E. B., Jr., and Little, J. M.: J. Pharm. & Exper. Therap. 119:161, 1957.

A. H. ROBINS CO., INC., Richmond 20, Virginia

It will pay you well to check and double check

Check these facts!

Baker's Modified Milk is a *complete* infant food — contains *all* requirements for complete infant nutrition . . . It is available in two time-saving forms — easy-to-prepare *Baker's Liquid* and *Baker's Powder,* the latter particularly adaptable for prematures and for complemental and supplemental feedings. Both forms are low in cost — less than a penny per ounce of formula.

Feeding Directions

BAKER'S MODIFIED MILK (Liquid)

NEWBORN INFANTS (Hospital)—1 part Baker's to 2 parts cool water.

FIRST WEEK AT HOME — 1 part Baker's to 1½ parts cool water.

AFTER FIRST WEEK AT HOME — 1 part Baker's to 1 part cool water.

Double Check the results you get!

In the hospital — and at home.

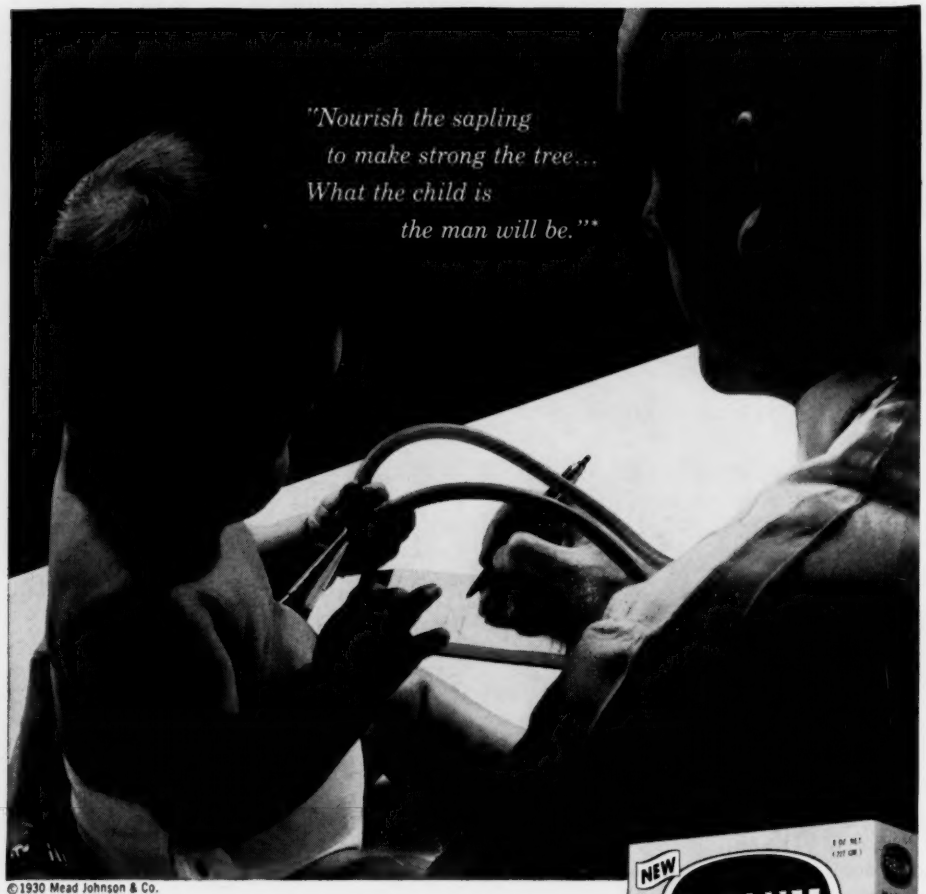
Liquid Powder

BAKER'S MODIFIED MILK

THE BAKER LABORATORIES, INC.

Milk Products Exclusively for the Medical Profession

***Main Office:* Cleveland 3, Ohio • *Plant:* East Troy, Wisconsin**



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Newest Pablum Cereal is 35% Protein

Pablum High Protein Cereal is derived from soy beans, oats, wheat and dried yeast. This new cereal food contains a level of active assimilable protein, 35%, much higher than that commonly present in cereal grains. It helps to keep baby trim. It satisfies baby's hunger over longer periods of time than even foods rich in carbohydrate.

Like all Pablum Cereals, Pablum High Protein Cereal is made by nutritional and pharmaceutical *specialists*.

You can specify PABLUM® *with confidence!*

Pablum Products DIVISION OF MEAD JOHNSON & CO., EVANSVILLE, IND. • Manufacturers of Nutritional and Pharmaceutical Products

NICOZOL

for senile psychoses

From
CONFUSION

to a
NORMAL
BEHAVIOR
PATTERN

NICOZOL relieves mental confusion and deterioration, mild memory defects and abnormal behavior patterns in the aged.

NICOZOL therapy will enable your senile patients to live fuller, more useful lives. Rehabilitation from public and private institutions may be accomplished for your mildly confused patients by treatment with the Nicozol formula. [1] [2]

NICOZOL is supplied in capsule and elixir forms. Each capsule or ½ teaspoonful contains:

Pentylenetetrazol . . 100 mg.
Nicotinic Acid . . . . . 50 mg.

1. Levy, S., *JAMA.*, 153:1260, 1953
2. Thompson, L., Procter R., *North Carolina M. J.*, 15:596, 1954

WRITE for **FREE NICOZOL**

DRUG SPECIALTIES, INC.
WINSTON-SALEM 1, N. C.

for professional samples of
NICOZOL capsules and literature on
NICOZOL for senile psychoses.

Income for the members of the North Carolina Medical Profession

Pays From The First Day of Medical Attention During Total Disability and Total Loss of Time Because of SICKNESS or ACCIDENT Originating After the Effective Dates of Coverages and For As Long As Total Disability, Total Loss of Time and Regular Medical Attention Continue

NOT FOR ONLY 26 WEEKS—NOT FOR ONLY 52 WEEKS BUT EVEN FOR YOUR ENTIRE LIFETIME!

House Confinement not required at any time.
Accidental loss of hands, feet or eyesight pays monthly benefits—not just a lump sum.

EXTRA BENEFITS—Double monthly benefits while you are hospitalized payable for as long as three months.
Cash benefits for accidental death.
Double income benefits if disabled in specified travel accident named in the policy.

OTHER IMPORTANT FEATURES—Waiver of Premium Provision. Limited Commercial Air Line Passenger Coverage. No Automatic Termination Age During Policy Period. A Special Renewal Agreement.

EFFECTIVE DATES OF COVERAGES—EXCEPTIONS

This policy covers accidents from Noon of the Policy date and sickness originating more than thirty days after the Policy Date, unless specifically excluded — except — the policy does not cover, and the premium includes no charge for loss which is caused by: war or any act of war or while in military service of any country at war; suicide or attempted suicide; insanity or mental derangement; travel outside the United States, Alaska or Canada (unless otherwise extended by rider) and aeronautics or air travel other than limited commercial air line passenger travel.

(MP 3208)

UNITED INSURANCE COMPANY OF AMERICA,
Lifetime Disability Income Dept.
301 East Boulevard, Charlotte 3, North Carolina.

I would like more information about your lifetime disability income protection.

I understand I will not be obligated.

Name..... Age.....

Address .....
or attached letterhead.

UNITED INSURANCE COMPANY OF AMERICA

Home Office: Chicago 5, Illinois

Mail coupon today while you are still healthy

FOR THE ENTIRE RANGE OF RHEUMATIC-ARTHRITIC DISORDERS—from the mildest to the most severe

many patients with MILD involvement can be effectively controlled with

'MEPROLONE'

many patients with MODERATELY SEVERE involvement can be effectively controlled with

'MEPROLONE'

NEW

and NOW for patients with SEVERE involvement

MULTIPLE COMPRESSED TABLETS

'MEPROLONE'

The first meprobamate-prednisolone therapy

the one antirheumatic, antiarthritic that simultaneously relieves: (1) muscle spasm (2) joint inflammation (3) anxiety and tension (4) discomfort and disability.

SUPPLIED: Multiple Compressed Tablets in three formulas: 'MEPROLONE'-5—5.0 mg. prednisolone, 400 mg. meprobamate and 200 mg. dried aluminum hydroxide gel. 'MEPROLONE'-2—2.0 mg. prednisolone, 200 mg. meprobamate and 200 mg. dried aluminum hydroxide gel. 'MEPROLONE'-1 supplies 1.0 mg. prednisolone in the same formula as 'MEPROLONE'-2.

MSD MERCK SHARP & DOHME
DIVISION OF MERCK & CO., INC.
PHILADELPHIA 1, PA.

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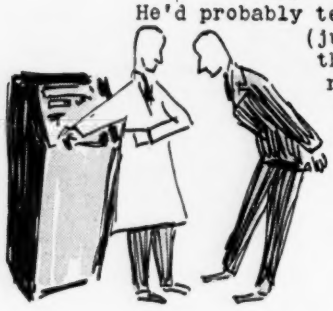
If you could visit

with a user of the Picker Anatomatic Century x-ray unit you'd soon know why this remarkable "new way in x-ray" machine has come so far so fast.

He'd probably tell you first how incredibly easy it is to use (just dial the body part and set its thickness... then press the button). He might sigh with relief at having no charts to consult, no calculations to make (the anatomatic principle does all the tedious "figgerin" for you).



He'd probably show you how good a radiograph he gets every time

He might even touch on the peace-of-mind that comes of having a local Picker office so near, with a trained Picker expert always on call for help and counsel

and there'd be no mistaking the light in his eye when it falls on the handsome big-name unit whose fine appearance adds so much to the impressiveness of his office.

P.S. Somewhere along the line the matter of price would come up ... he'd most likely comment on how little he paid to get so much. Or he might even be among those who rent their x-ray machine (Picker has an attractive rental plan, you know).

P.P.S. Next best thing is to call your local Picker man in and let him tell you about this great new machine (find him in your 'phone book) or write Picker X-Ray Corporation, 25 South Broadway, White Plains, N. Y.

Current Concepts in

Feeding Newborns

Successful infant feeding depends on effective planning of the newborn's nutritional regimen. The first feeding, 12 hours after birth, may consist of a prelacteal solution of KARO® Syrup. This should be offered in one or two ounce amounts at two hour intervals for 24 to 48 hours to fulfill the high water requirement during the first week of life. Breast feeding may be initiated on the second day for five minute intervals to obtain colostrum and stimulate breast secretion. However, the prelacteal feeding is continued thereafter and between nursings.

Artificial feeding is offered on the second day if breast feeding is denied. Small infants are fed at three hour intervals and large infants at four hour intervals. The initial formula usually is a low caloric milk mixture to enable gradual adaptation of the feeding to the infant's tolerance. Concentration of the formula is gradually increased at intervals of several days, in the absence of digestive disturbances. The infant should be fed in a semi-reclining position, burped during and after feeding, and kept on his right side or abdomen undisturbed for an hour.

The same problems of infant feeding recur from generation to generation, but solutions may differ with each era. The carbohydrate requirement for all infants is as completely fulfilled by KARO Syrup today as a generation ago. Whatever the type of milk adapted to the individual infant, KARO Syrup may be added confidently because it is a balanced mixture of low molecular weight sugars, readily miscible, well tolerated, palliative, hypoallergenic, resistant to fermentation in the intestine, easily digestible, readily absorbed and non-laxative. It is readily available in all food stores.

℞ FIRST FORMULAS FOR NEWBORNS ADAPTED ACCORDING TO TOLERANCE

FORMULA I .....11 cals./oz.
*Whole Milk ..... 8 oz.
Water .....12 oz.
Karo .....½ oz.
3½ oz. x 6 q 4h.

FORMULA I .....12.5 cals./oz.
**Evap. milk ..... 4 oz.
Water .....14 oz.
Karo .....½ oz.
3½ oz. x 6 q 4h.

FORMULA I .....11 cals./oz.
Dried milk .....4 tbsp.
Water .....20 oz.
Karo .....½ oz.
3½ oz. x 6 q 4h.

FORMULA III .....16 cals./oz.
Whole milk .....10 oz.
Water .....10 oz.
Karo ..... 1 oz.
3½ oz. x 6 q 4h.

FORMULA III .....20 cals./oz.
Evap. milk ..... 6 oz.
Water .....12 oz.
Karo ..... 1 oz.
3 oz. x 6 q 4h.

FORMULA III .....18 cals./oz.
Dried milk .....6 tbsp.
Water .....20 oz.
Karo ..... 1 oz.
3½ oz. x 6 q 4h.

FORMULA II .....13.5 cals./oz.
Whole milk ..... 9 oz.
Water .....11 oz.
Karo .....¾ oz.
3½ oz. x 6 q 4h.

FORMULA II .....16 cals./oz.
Evap. milk ..... 5 oz.
Water .....13 oz.
Karo .....¾ oz.
3 oz. x 6 q 4h.

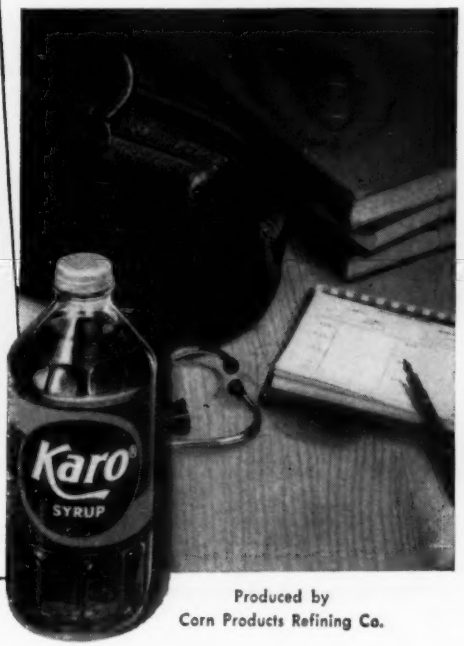
FORMULA II .....14.5 cals./oz.
Dried milk .....5 tbsp.
Water .....20 oz.
Karo .....¾ oz.
3½ oz. x 6 q 4h.

*Whole lactic acid milk formulas may also be prepared from whole cow's milk.

**Whole lactic acid milk formulas may also be prepared from evaporated cow's milk.

Adapted from Nelson's Pediatrics, Saunders, Phila. 1954

MEDICAL DIVISION
CORN PRODUCTS REFINING CO.
17 Battery Place, New York 4, N. Y.



Produced by
Corn Products Refining Co.

in spasticity of the GI tract

Pavatrine®
125 mg.
with Phenobarbital
15 mg.

- *is an effective dual antispasmodic*
- *combining musculotropic and neurotropic action plus mild central nervous system sedation for "the butterfly stomach."*

dosage: one tablet before each meal and at bedtime.

SEARLE

PHENAPHEN® PLUS

Phenaphen Plus is the physician-requested combination of **Phenaphen,** plus an antihistaminic and a nasal decongestant.

Available on prescription only.

Robins

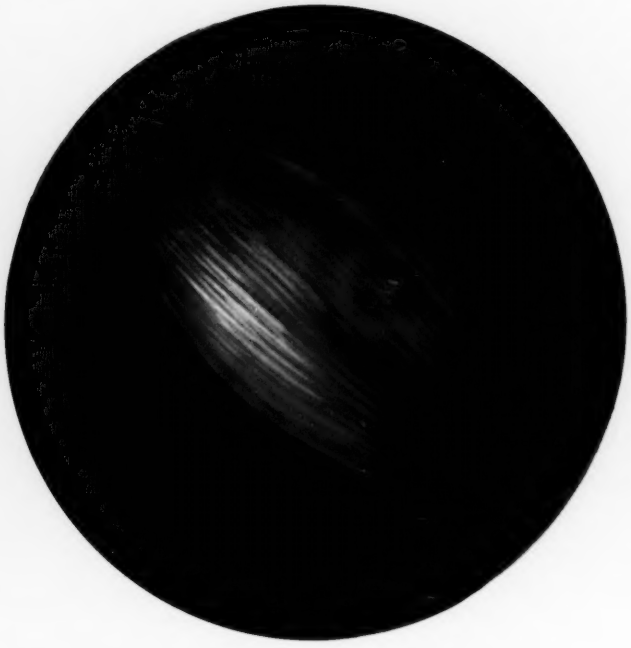
each coated tablet contains:	**Phenaphen**
Phenacetin (3 gr.)	194.0 mg.
Acetylsalicylic Acid (2½ gr.)	162.0 mg.
Phenobarbital (¼ gr.)	16.2 mg.
Hyoscyamine Sulfate	0.031 mg.
	plus
Prophenpyridamine Maleate	12.5 mg.
Phenylephrine Hydrochloride	10.0 mg.

For anxiety, tension and muscle spasm in everyday practice.

- well suited for prolonged therapy
- well tolerated, relatively nontoxic
- no blood dyscrasias, liver toxicity, Parkinson-like syndrome or nasal stuffiness

RELAXES BOTH MIND AND MUSCLE

WITHOUT IMPAIRING MENTAL OR PHYSICAL EFFICIENCY



Miltown®

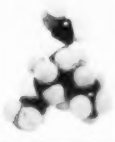
tranquilizer with muscle-relaxant action

2-methyl-2-**n**-propyl-1,3-propanediol dicarbamate — U. S. Patent 2,724,720

Supplied: 400 mg. scored tablets
200 mg. sugar-coated tablets

Usual dosage: One or two 400 mg. tablets t.i.d.

Literature and samples available on request



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DISCOVERED & INTRODUCED BY
WALLACE LABORATORIES
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CM.5099-R

AN IMPORTANT ADVANCE IN ESTROGEN-ANDROGEN THERAPY

Because it replaces *half* control with *full* control.

Because it treats the *whole* menopausal syndrome.

Because *one* prescription manages *both* the psychic and somatic symptoms.

SUPPLIED: Bottles of 60 tablets.
Each tablet contains:

MILTOWN® (meprobamate, Wallace) ..... **400 mg.**
2-methyl-2-*n*-propyl-1,3-propanediol dicarbamate.
U. S. Patent No. 2,724,720.

Conjugated Estrogens (equine) ..... **0.4 mg.**
Licensed under U. S. Patent No. 2,429,398.

DOSAGE: One tablet t.i.d. in 21-day courses with one week rest periods. Should be adjusted to individual requirements.

Samples and literature on request.

Two-dimensional treatment of the menopause

"Milprem"

MILTOWN® A Proven Tranquilizer + CONJUGATED ESTROGENS (EQUINE) A Proven Estrogen

WALLACE LABORATORIES, *New Brunswick, N. J.*
who discovered and introduced Miltown, the original meprobamate.

Westbrook Sanatorium

RICHMOND · · · Established 1911 · · · VIRGINIA

A private psychiatric hospital employing modern diagnostic and treatment procedures—electro shock, insulin, psychotherapy, occupational and recreational therapy—for nervous and mental disorders and problems of addiction.

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when anxiety and tension "erupts" in the G. I. tract...

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PATHIBAMATE*

Meprobamate with PATHILON® Lederle

Combines Meprobamate (*400 mg.*) the most widely prescribed tranquilizer . . . helps control the "emotional overlay" of duodenal ulcer — without fear of barbiturate loginess, hangover or habituation . . . *with* PATHILON (*25 mg.*) the anticholinergic noted for its extremely low toxicity and high effectiveness in the treatment of many G.I. disorders.

Dosage: 1 tablet t.i.d. at mealtime. 2 tablets at bedtime. *Supplied:* Bottles of 100, 1,000.

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Lederle

LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, NEW YORK

NEW... intranasal synergism

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Biosynephrine
TRADEMARK

Nasal Spray
15 cc.

Contains:

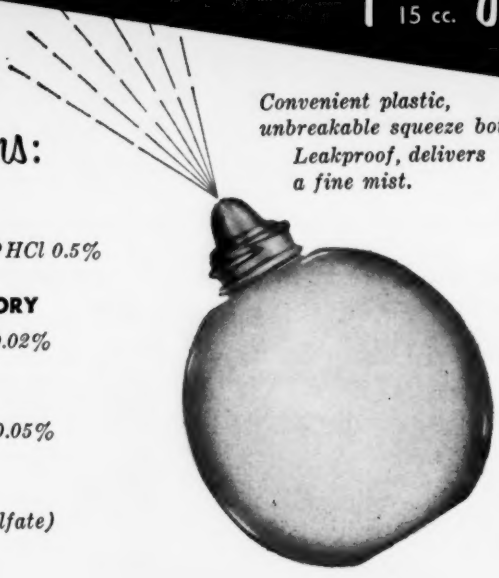
DECONGESTIVE
Neo-Synephrine® HCl 0.5%

ANTI-INFLAMMATORY
Hydrocortisone 0.02%

ANTI-ALLERGIC
Thenfadil® HCl 0.05%

ANTIBACTERIAL
Neomycin (as sulfate) 0.6 mg./cc.

Polymyxin B (as sulfate) 3000 u/cc.



Convenient plastic, unbreakable squeeze bottle. Leakproof, delivers a fine mist.

POTENTIATED ACTION for better clinical results

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outstanding appetite stimulant

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LYSINE-VITAMIN SUPPLEMENT LEDERLE

Problem-eaters, the underweight, and generally below-par patients of all ages respond to INCREMIN.

INCREMIN offers l-Lysine for protein utilization, and essential vitamins noted for outstanding ability to stimulate appetite, overcome anorexia.

Specify INCREMIN in either Drops (cherry flavor) or Tablets (caramel flavor). Same formula. Tablets, highly palatable, may be orally dissolved, chewed, or swallowed. Drops, delicious, may be mixed with milk, milk formula, or other liquid; offered in 15 cc. polyethylene dropper bottle.

Each INCREMIN Tablet
or each cc. of INCREMIN Drops *contains:*

l-Lysine	300 mg.	Pyridoxine (B_6)	5 mg.
Vitamin B_{12}	25 mcgm.	(INCREMIN Drops contain 1% alcohol)	
Thiamine (B_1)	10 mg.		

Reg. U. S. Pat. Off.

Dosage only 1 INCREMIN TABLET or 10-20 INCREMIN Drops daily.

Lederle

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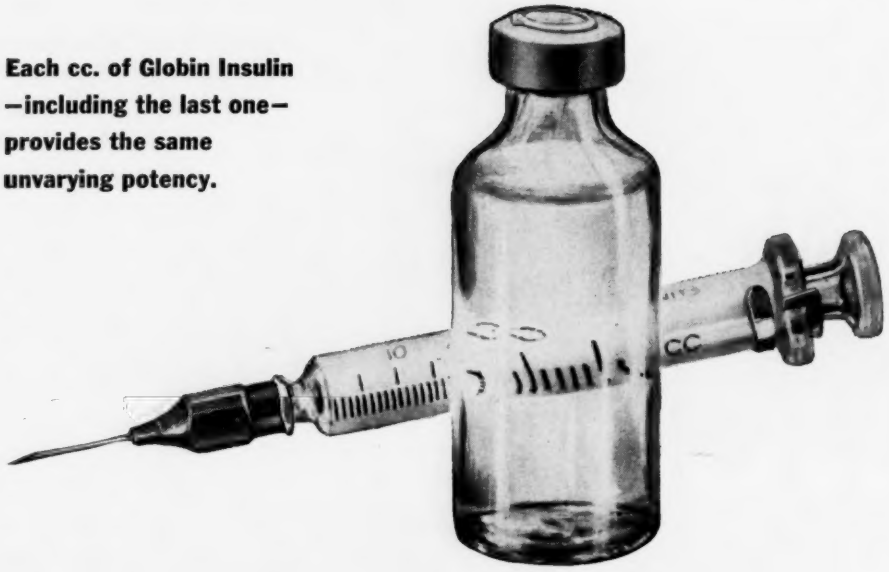
Avoid "BOTTOM OF THE VIAL" reactions

Each cc. of Globin Insulin —including the last one— provides the same unvarying potency.



Of the intermediate-acting insulins, only Globin Insulin is a clear solution.

24-hour control for the majority of diabetics

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BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York

NOW—EFFECTIVE STEROID HORMONE THERAPY OF RHEUMATIC AFFECTIONS WITH GREATER SAFETY AND ECONOMY

PABALATE-HC

Robins

Pabalate with Hydrocortisone

Clinical evidence indicates that, in Pabalate-HC, the synergistic antirheumatoid effects of hydrocortisone, salicylate, para-aminobenzoate, and ascorbic acid achieve satisfactory remission of symptoms in *up to 85% of cases studied*

—with a much higher degree of safety

—even when therapy is maintained for long periods

—at significant economy for the patient

Each tablet of Pabalate-HC contains 2.5 mg. of hydrocortisone—50% more potent than cortisone, yet not more toxic.

FORMULA

In each tablet:

Hydrocortisone (alcohol)	2.5 mg.
Potassium salicylate	0.3 Gm.
Potassium para-aminobenzoate	0.3 Gm.
Ascorbic acid	50.0 mg.

DOSAGE: Two tablets four times daily. Additional information on request.

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Ethical Pharmaceuticals of Merit since 1878

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ESTABLISHED — 1916

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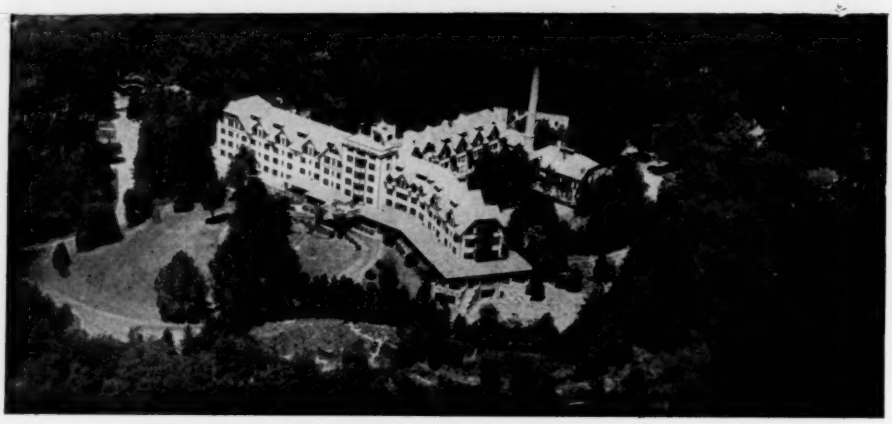

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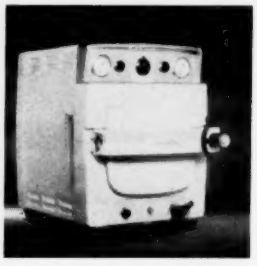

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Speed — Ultra fast! Double shell provides stand-by steam reserve for day-long sterilizing readiness . . . without waiting.

Safety — Foolproof! Safety door, safety fill, safety timer, safety valve and cut-off . . . plus all-important safety to your patients.

Convenience — A joy to own! Big 9x16 inch chamber, bulk supply rack, two oversized trays, one 8½x15 inches.

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CLINICAL COLLOQUY

My patients complain that
the effect of the pain tablet I prescribe
often wears off in less than 3 hours.

***Why not try the new analgesic
that gives faster,
longer-lasting pain relief?***

You mean something that
doesn't require repeat dosage so often?

***Yes—it's called Percodan.®
It not only works in 5 to 15 minutes but
one tablet sustains its pain-relieving effect
for 6 hours or longer!***

How about side effects?

***No problem. For example,
the incidence of constipation
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Sounds worth trying—what's the average adult dose?

One tablet every 6 hours. That's all.

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• **allays bronchial spasm** • **liquefies tenacious secretions** • **suppresses allergic manifestations**

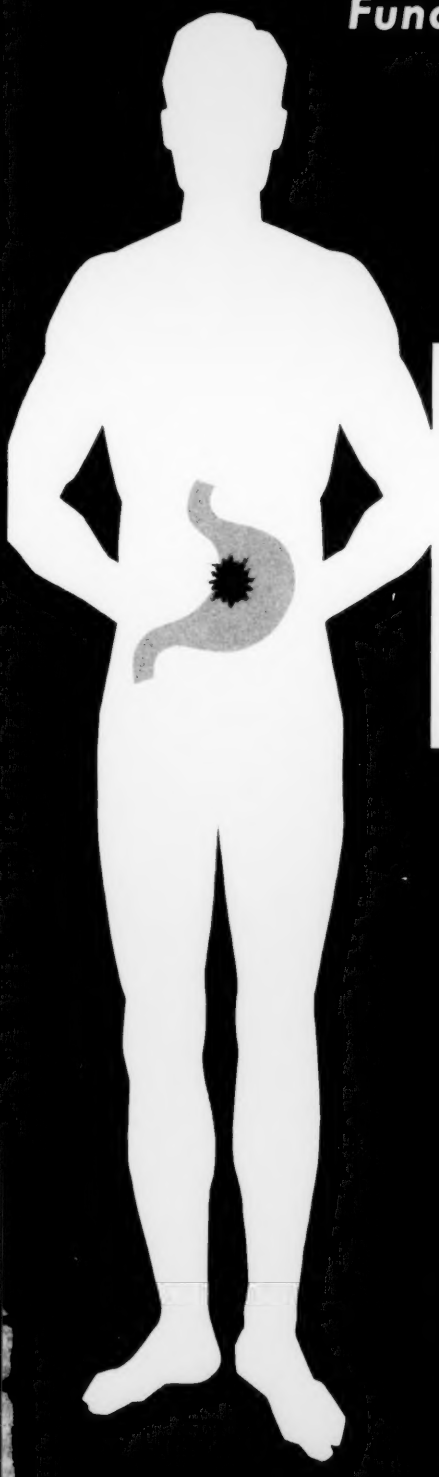
The ingredients of Hydryllin Compound are proportioned to provide high therapeutic response.

Each 4 cc. (one teaspoonful) contains:

Aminophyllin	32.0 mg.	Chloroform	8.0 mg.
Diphenhydramine	8.0 mg.	Sugar	2.8 Gm.
Ammonium chloride	30.0 mg.	Alcohol 5% (v/v)	

G. D. Searle & Co., Chicago 80, Illinois.

SEARLE *Research in the Service of Medicine*



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Irritability and Tension

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TABLETS

Potent ANTISECRETORY • ANTICHOLINERGIC • SEDATIVE

Each tablet contains:

Monodral bromide	5 mg.
Mebaral	32 mg.

Dependable control of hyperacidity and hypermotility. Spasmolysis. Prompt and prolonged pain relief. Tranquillity without drowsiness.

Peptic ulcer, 1 or 2 tablets three or four times daily. Other gastro-intestinal disorders, 1 tablet three or four times daily.

Bottles of 100 tablets.

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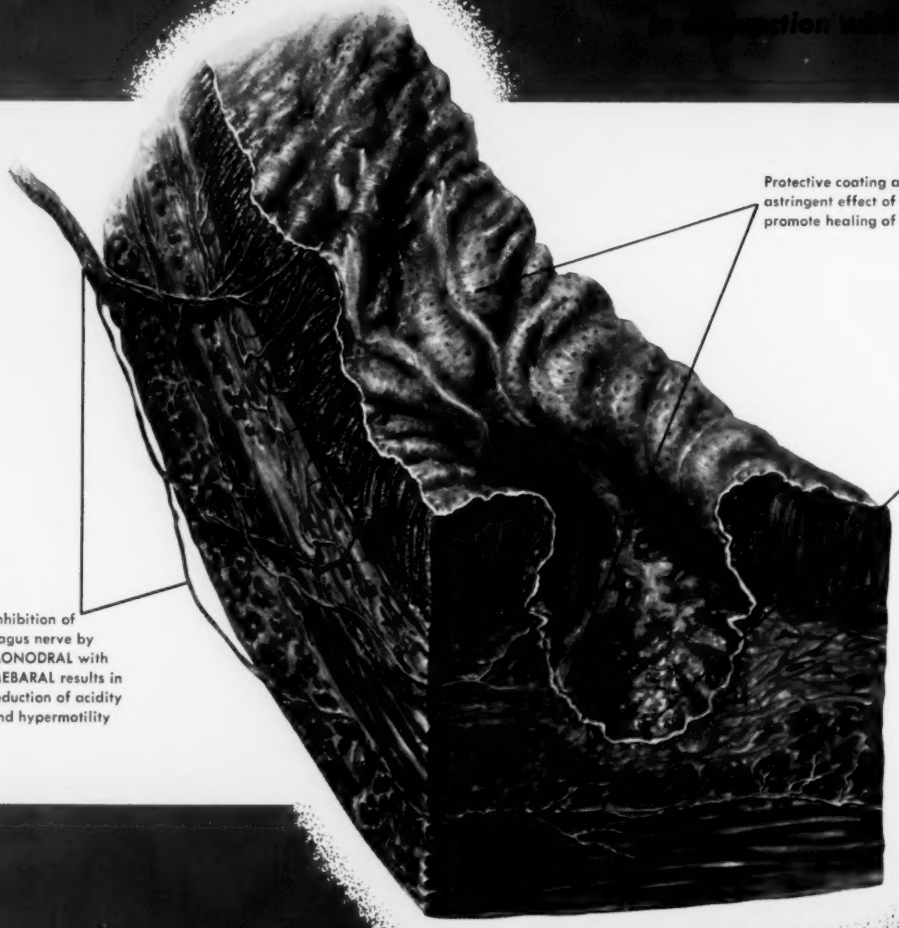
Protective Coating with

Creamalin

FAST-ACTING PROTECTIVE GEL

For best results in PEPTIC ULCER


Protective coating and mild astringent effect of CREAMALIN promote healing of peptic ulcer.
CREAMALIN
Inhibition of vagus nerve by MONODRAL with MEBARAL results in reduction of acidity and hypermotility

DOSE:

From 2 to 4 teaspoonfuls Creamalin

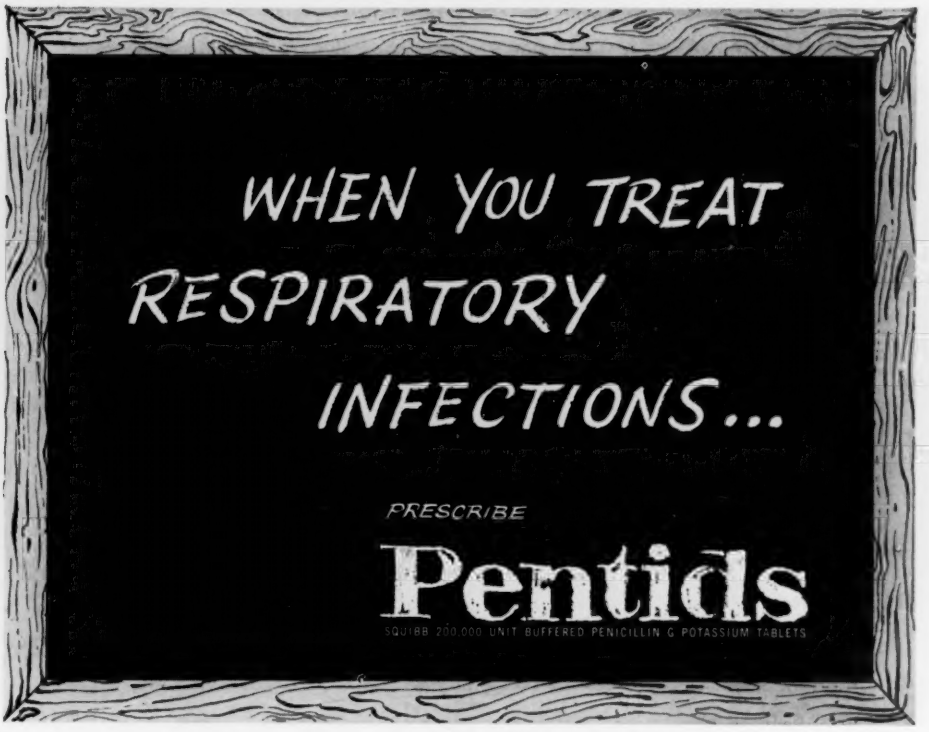
or from 2 to 4 Creamalin

chewed) every two to three

small amount of water

Winthrop

Creamalin (brand of aluminum hydroxide gel)
and Mebaral (brand of mephobarbital)



- *six years of experience with Pentids in millions of patients confirm clinical effectiveness and safety*
- *excellent results with 1 or 2 tablets t.i.d. for many common bacterial infections*
- *may be given without regard to meals*
- *economical . . . Pentids cost less than other penicillin salts*

Just 1 or 2 tablets t.i.d. Bottles of 12, 100 and 500

NEW! PENTIDS FOR SYRUP. Orange flavored powder which, when prepared with water, provides 60 cc. of syrup with a potency of 200,000 units of penicillin G potassium per 5 cc. teaspoonful.

Also available: Pentids Capsules, Pentids Soluble Tablets. Pentid-Sulfas.

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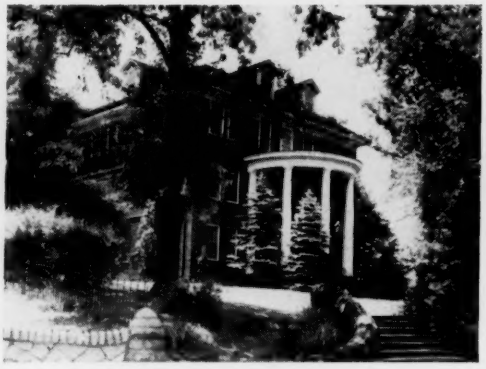

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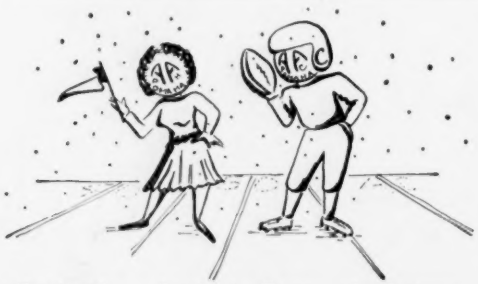

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based on thousands of case histories:

25 *mg. (q.i.d.)*

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perhaps the safest ataraxic known

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Supplied: In tiny 10 mg. (orange) and 25 mg. (green) tablets. Also now available in 100 mg. tablets. Bottles of 100. ATARAX Syrup, 10 mg. per tsp., in pint bottles. Prescription only.

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ATARAX® PARENTERAL SOLUTION
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In daily practice: always have it handy
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- to make overwrought patients manageable without loss of alertness
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Available on prescription only.

Robins

each coated tablet contains:	**Phenaphen**
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Hyoscyamine Sulfate	0.031 mg.
plus	
Prophenpyridamine Maleate	12.5 mg.
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In the nonhormonal treatment of arthritis and allied disorders no agent surpasses BUTAZOLIDIN in potency of action.

Its well-established advantages include remarkably prompt action, broad scope of usefulness, and no tendency to development of drug tolerance. Being nonhormonal, BUTAZOLIDIN causes no upset of normal endocrine balance.

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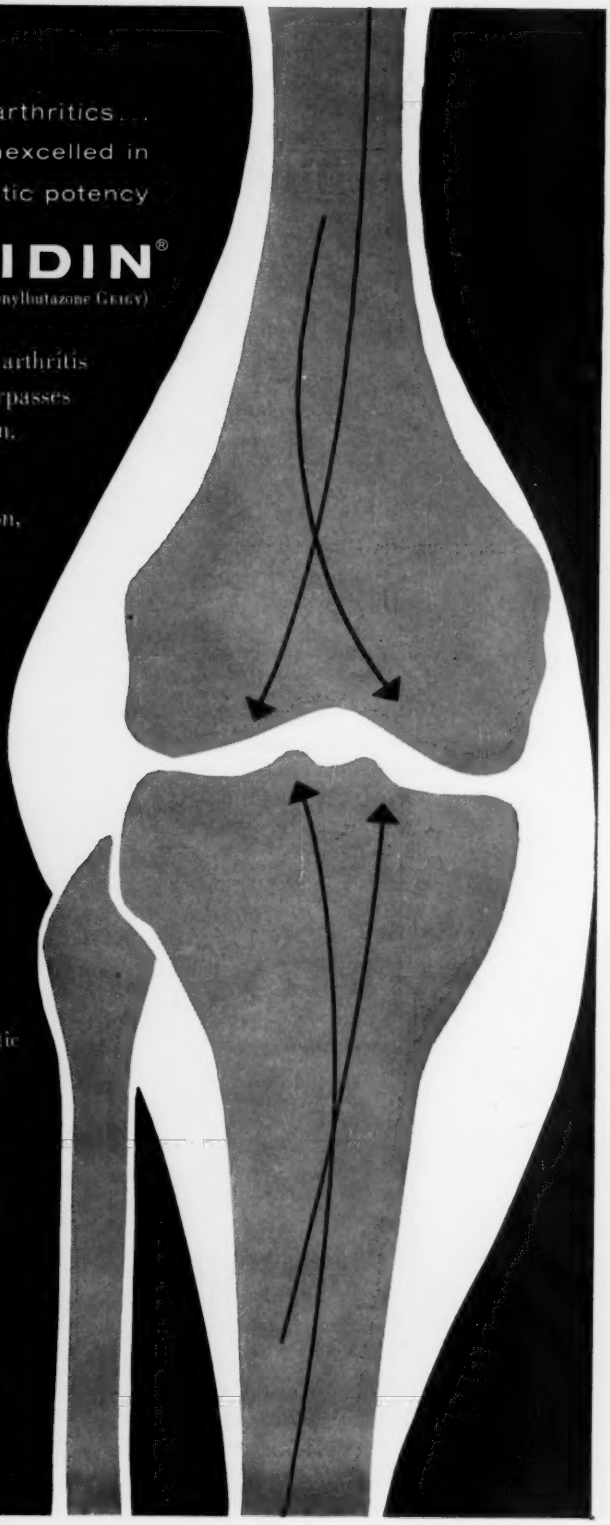

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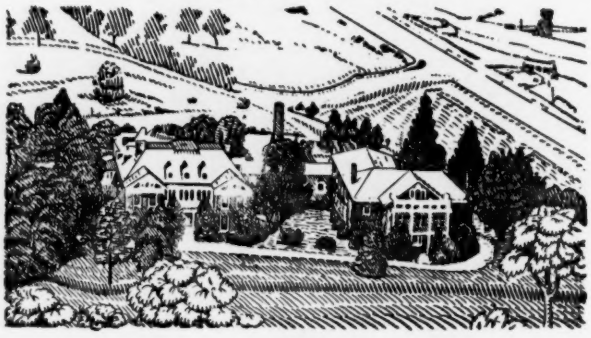

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when anxiety and tension "erupts" in the G. I. tract...

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Meprobamate with PATHILON® Lederle

Combines Meprobamate (*400 mg.*) the most widely prescribed tranquilizer . . . helps control the "emotional overlay" of ileitis — without fear of barbiturate loginess, hangover or habituation . . . *with* PATHILON (*25 mg.*) the anticholinergic noted for its extremely low toxicity and high effectiveness in the treatment of many G.I. disorders.

Dosage: 1 tablet t.i.d. at mealtime. 2 tablets at bedtime. *Supplied:* Bottles of 100, 1,000.

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Helen B. Taussig, M.D.
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E. Grey Dimond, M.D.,
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Associate Professor of Medicine, Northwestern University, Chicago, Illinois.

Tuition fee: $100.00

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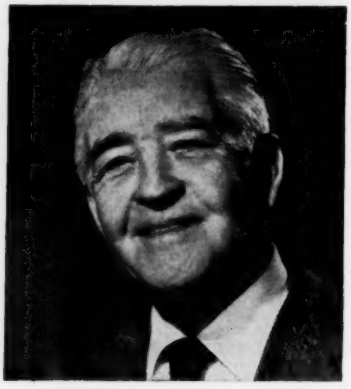

years ago they told me:

"YOU HAVE LESS THAN A YEAR TO LIVE!"

"MUST HAVE BEEN back in 1919 or '20. Hopeless case of diabetes. No known cure . . .

"BUT HERE I AM. They found a treatment—insulin—in time. Today, *nobody* has to die of diabetes.

"CANCER, I know, is a tougher problem. But the laboratories can lick that one, too—with our support. Already, they're curing people who would have been done for a few years ago. Last year—thanks to $5,000,000 allocated by the American Cancer Society from our contributions—they found out a lot more . . . though there's still a long way to go.

"THEY NEED MONEY, though. $5,000,000 is still less than 4 cents per American *per year*. Not enough. Not enough to find the answer *fast* enough—230,000 Americans are going to die of cancer *this year*, they say.

"I'M NOT RICH, but I gave 'em $50 last year—hope to do better this time. After all, where would *I* be if the laboratories working on diabetes, that time, hadn't been given enough support—?"

Cancer
MAN'S CRUELEST ENEMY
Strike back—Give

THIS DR

is the **symbol**
of the
Standardized
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Quinidine Sulfate
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0.2 Gram
(approx. 3 grains)
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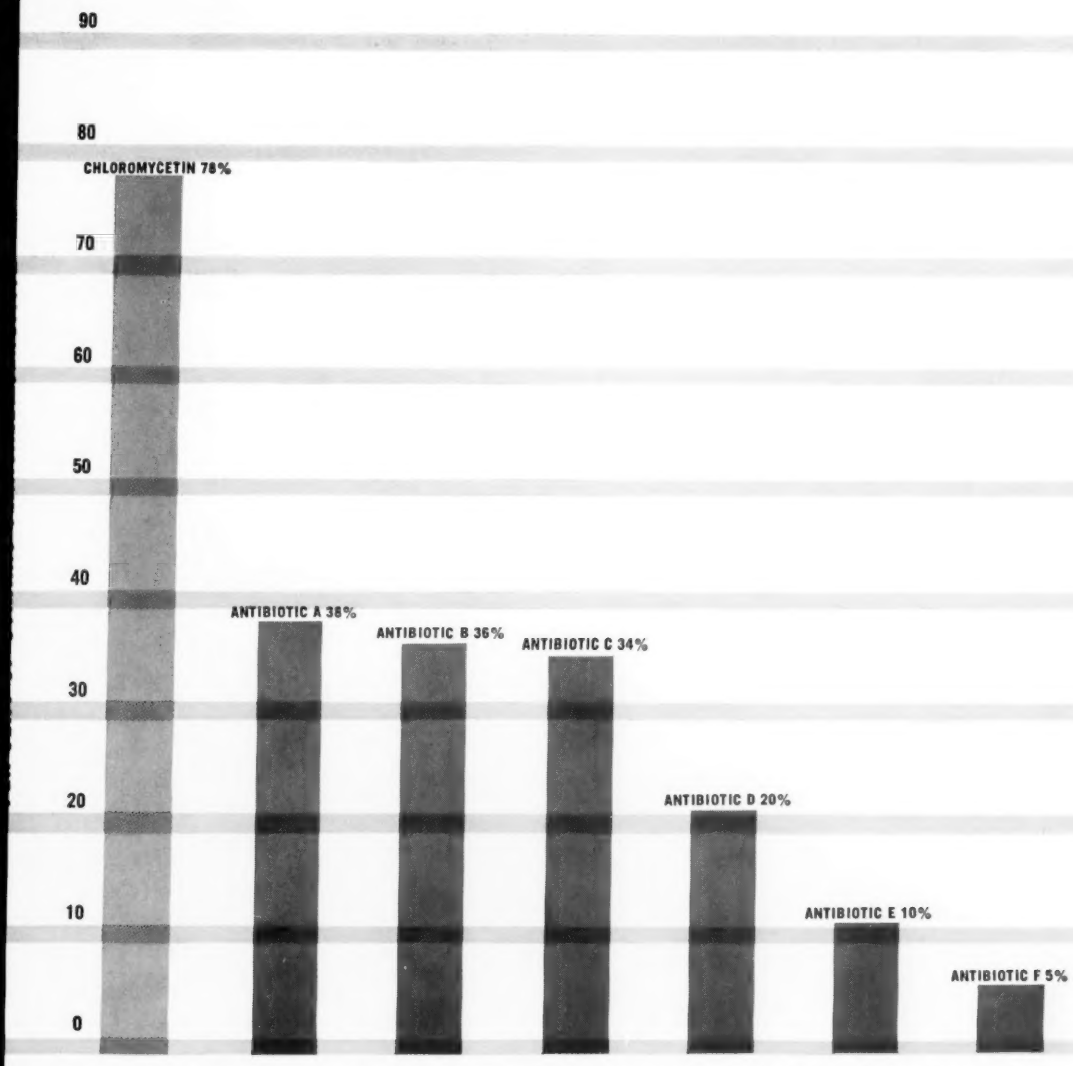
COMPARATIVE SENSITIVITY OF MIXED PROTEUS SPECIES TO CHLOROMYCETIN AND SIX OTHER WIDELY USED ANTIBIOTIC AGENTS*

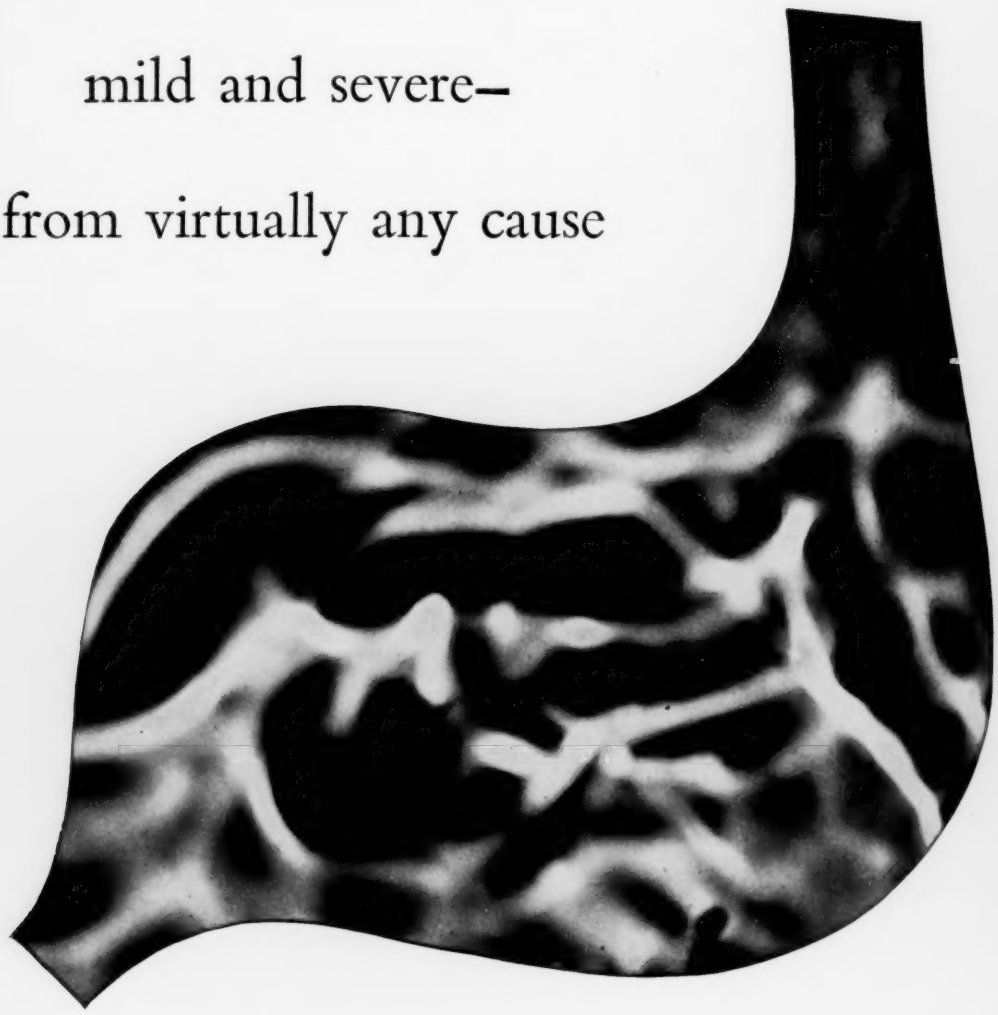


*This graph is adapted from Waisbren and Strelitzer.[15] It represents *in vitro* data obtained with clinical material isolated between the years 1951 and 1956. Inhibitory concentrations, ranging from 3 to 25 mcg. per ml., were selected on the basis of usual clinical sensitivity.

stops nausea and vomiting–

mild and severe–

from virtually any cause



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